Author’s response to reviews

Title: Nutraceutical approach to moderate cardiovascular risk with a combination containing the probiotic Bifidobacterium longum BB536 and red yeast rice extract - a randomized, double-blind, placebo-controlled study

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Reviewer #2: I am really grateful to the Editor for making me read such an original paper reporting really interesting data. I think that this manuscript is extremely well written and the Authors have to be complimented for this.

R. The authors thank the reviewer for these comments.

Some minor comments to be addressed by Ruscica and his Collaborators:
- Please, specify that the trial was parallel-group designed (line 73).

R. Thanks, done.

- In my opinion, "patients of both sexes" (line 93) should be removed from the inclusion criteria of the study since it is not useful at all.

R. Thanks, done.

- Please, remove the sentence "All patients were in primary CV prevention and free from liver/kidney disorders potentially affecting the response to treatment and were not on any drug affecting lipid/lipoproteins or glycemic profile, including thiazolidinediones or corticosteroids" (line 94-96) from the method paragraph (indeed, this is a description of the study sample and for this reason it could be more appropriate in the results paragraph of the manuscript) and complete the inclusion and the exclusion criteria of the study by specifying that only subjects in primary prevention for CV disease were enrolled.

R. Thanks, the sentence was removed from line 94-96 and these observations were added in the results section. Moreover, in the inclusion and the exclusion criteria of the study we specified that only subjects in primary prevention for CV disease were enrolled.

- Table 1 reports a significant p-value for difference in age between the study groups at baseline. Could this significant difference have influenced the subjects response to the tested treatment and, finally, the study findings?

R. Thanks for this important question. As reported in the Statistical analysis section, all the differences in change by arms were evaluated by ANCOVA models adjusted for baseline values and age. Mixed effects models, used to take into consideration correlation within subjects and to assess changes in time, are also adjusted for baseline value for age.

Thus, the potential impact of this age difference has been considered in our statistical analysis.

- Please, in the discussion section refer to doi:10.1007/s12325-017-0580-1 and doi:10.1002/ptr.6282, which are two papers of interest in the field.

R. Thanks, reference to these two papers has been added.