Reviewer’s report

Title: Youth Depression Alleviation with Anti-inflammatory Agents (YoDA-A): A Randomised Clinical Trial of Rosuvastatin and Aspirin

Version: 0 Date: 20 Sep 2019

Reviewer: Michele Fornaro

Reviewer's report:

Re: Youth Depression Alleviation with Anti-inflammatory Agents (YoDA-A): A Randomised Clinical Trial of Rosuvastatin and Aspirin

1) The primary outcome of the study was "change in MADRS" score at w12 vs. baseline. I would also suggest to append the rate of responders defined as the proportion of cases who achieved at least a 50% score reduction vs. baseline records, since I think that would be more informative than the SMD indexes (which, by the way, I did not see reported). Thank you.

2) I think the discussion should further stress-out the fact that anti-inflammatory agents for depression could be used at low-to-moderate doses when prescribed as augmentation strategies for established antidepressants (e.g. previous reports for sertraline add-on), even when monoamine-modulating antidepressant do not lead to satisfactory responses. This is something to study in forthcoming RCTs comparing an antidepressant plus placebo or plus an anti-inflammatory agent. Ideally, that may also save some dose of the augmentation agent, thus resulting in lower discontinuation rate attributed to side effect (tolerability).

3) I appreciated the GEE option instead of the GLM and the explanation why.

4) The computed sample size is 270 or more, however 130 were randomized.

Overall, I really enjoyed reading the present report, which I found impeccable, especially in terms of methodology and interpretation of the results. Therefore, my remarks should be merely intended as discretional suggestions for the authors, to whom I compliment for their efforts.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

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If not, please specify which controls are required in your comments to the authors.

Yes
Are the conclusions drawn adequately supported by the data shown?
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