Reviewer's report

Title: Antiviral Treatment Perspective against Borna disease virus 1 infection in Major Depression: A Double-Blind Placebo-Controlled Randomized Clinical Trial

Version: 2 Date: 20 Sep 2019

Reviewer: Research Square

Reviewer's report:

STATISTICAL REVIEWER ASSESSMENT:

Is the study design appropriate for the research question (considering whether the analyzed population accurately reflects the design and whether you see any problems with control/comparison groups, e.g., likely confounders)?

Yes - overall design, population, and control groups are appropriate

Are methodologies adequate and well implemented (considering whether assumptions are addressed and whether analyses are robust)?

Yes - methodologies are adequate and well implemented, assumptions are addressed, analysis is robust

Are the analyses adequately communicated (considering whether reporting details are adequate and whether figures and tables are well labeled and described)?

Yes - important reporting details are present, analyses are adequately communicated, figures and tables are well labeled and described

Does the interpretation accurately reflect the analyses without overstatement (considering whether limitations/bias are acknowledged and whether accurate descriptors, e.g., 'significant', are used)?

Yes - interpretation accurately reflects analyses, limitations/bias are acknowledged, accurate descriptors are used
Could an appropriately REVISED version of this work represent a statistically sound contribution?

Yes - current version has sound statistics

STATISTICAL REVIEWER COMMENTS:

This is a well-designed and analysed RCT study that demonstrated a possible practice-changing in mental health care.

The drawback of the study designed included cross over study design instead of, e.g. parallel-group and limited participants in this Phase II trial have been pointed out and discussed by the Authors.

The statistical analyses were performed adequately.

REQUESTED REVISIONS:

This is a well-written manuscript. There are a couple of minor questions.

1. Line 154 - 155: "The post-trial follow-up period of 12 months with optional amantadine treatment up to 300 mg/d was completed by 29 remaining patients." What was the reason that amantadine treatment changed from "200 mg/d" to "up to 300 mg/d"?

2. Line 221: what is "(CAG)"? Perhaps PAG? Don't think CAG has been defined previously.

3. Line 298: Please provide SPSS software version.

4. Line 745: The "BDV" next to the "AB" should be deleted.

5. I'm curious, for the participants and the researchers were they aware that this is a cross-over study? I.e. regardless of which group that patients been randomly selected, they will eventually receive amantadine?

6. The half-life for amantadine is up to 31 h. In terms of carrying over effect, I think it should be more specifically related to amantadine, which is a curative treatment.

7. Authors should include a table similar to Table 2 but with separated data for Amantadine and Placebo treatment groups from Period I and II (Figure 1). It would be interesting to see if Amantadine treatment in Period I has any impact on the Placebo effect from Period II.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
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?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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