Reviewer’s report

Title: Fingolimod after a first unilateral episode of acute optic neuritis (MOVING) – Preliminary results from a randomized, rater-blind, active-controlled, phase 2 trial

Version: 0 Date: 13 Nov 2019

Reviewer: Tim Sinnecker

Reviewer's report:

The authors report preliminary results from an investigator-driven clinical trial that was discontinued due to poor recruitment. The study was inspired by preclinical data suggesting that fingolimod may have an impact on cellular pathways involved in remyelination and/or repair. In addition, the visual system is ideal to study pathophysiological mechanisms and/or treatment effects, as it is easily accessible and well characterized. On this background, the authors aimed to investigate pro-regenerative effects of fingolimod on the optic nerve after acute unilateral optic neuritis. Although outcome analyses were only available from 9 participants, which limit the generalizability and interpretation of the results, I favour a publication of the results as i) the study had a clear and important null hypothesis, ii) the study design was appropriate to shed light on the hypothesis, iii) the manuscript reports (missing) outcome parameters, group differences at baseline as well as AEs in a transparent and well structured manner, and iv) sample size calculations were performed based on available data that may guide future studies.

I have only minor comments in order to improve the manuscript:

- In the abstract and supplementary tab. 1 the authors state that they have accessed the number of clinical relapses. In the results section, it is only stated that 2 fingolimod patients sustained relapses. Can the authors give more details? Were clinical relapses observed within the IFN group?

- The authors state that they have analysed the cumulative number of T2 lesions and the corresponding lesion volume at baseline and 6 months of follow-up. Why didn't the authors assessed the number/volume of new and/or enlarging T2 lesions as this measure would provide important information on subclinical disease activity which may interfere with the primary outcome parameter (mfVEP latency)? Also, did the authors assessed subclinical damage to the posterior visual pathways (e.g. optic radiation lesions)?

- the authors provided a well balanced conclusion and interpretation of their findings at the end of the discussion section; it would be worthwhile to add some of these ideas (e.g. deterioration of the control group, small number of complete observations) to the conclusion of the abstract.
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 recommend additional statistical review

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

Acceptable

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6: Although I have conducted and published other studies in collaboration with some of the co-authors, I was not involved and not aware of the reviewed study.

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