Author's response to reviews

**Title:** Controversies in Neurology: why Monoamine Oxidase B Inhibitors Could Be A Good Choice for the Early Treatment of Parkinson's Disease

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Author's response to reviews: see over
Dear editors of BMC Neurology,

today we would like to submit the revision of our manuscript entitled:

“Controversies in Neurology: why Monoamine Oxidase B Inhibitors Could Be A Good Choice for the Early Treatment of Parkinson's Disease”.

We appreciate the helpful review and all comments that have been made by the editor and the reviewers, which subsequently have been used by us to modify the original manuscript. As requested we have uploaded the manuscript with all changes tracked electronically. In the following, we would like to give a summary of all changes that have been made in response to the reviewer comments on a point-by-point basis:

Comments by the editor:

The authors have adjusted the cover page in order to meet the required format for BMC Neurology. Moreover, the abstract was structured into sections as suggested by the editors. The title has been slightly modified to support the now more objective discussion in the text.

Comments by reviewer Lawrence Elmer:

Possible dietary tyramine-induced hypertensive crisis and serotonin syndrome in MAO-B treated patients have been embedded and are now extensively discussed in the safety section of the manuscript. We have also considered the reference (Goren et al., 2010), which was kindly suggested to us by the reviewer.

Comments by reviewer Laszlo Vecsei:

The authors acknowledge the inferiority of symptomatic efficacy in MAO-B inhibitors, which had not been emphasized previously since the manuscript was originally thought to serve as positional paper for MAO-B inhibitors as part of a Pro/Con debate. In the revised version, we have therefore outlined the
symptomatic inferiority of this substance class in comparison to dopamine agonists and levodopa and have modified the abstract, motor section as well as the conclusion accordingly.

In the conclusions, we have now furthermore stated that head-to-head comparison of individual drugs would be helpful to make a final conclusion on how to treat initially and mentioned the currently running PD MED trial, which is a patient-orientated approach coming close to this objective.

Comments by reviewer Oren S Cohen:

- Section 1:
As already mentioned in response to the comments by reviewer Laszlo Vecsei, the authors acknowledge the inferiority of symptomatic efficacy in MAO-B inhibitors, which had not been emphasized previously since the manuscript was originally thought to serve as positional paper for MAO-B inhibitors as part of a Pro/Con debate. In the revised version, we have therefore outlined the symptomatic inferiority of this substance class in comparison to dopamine agonists and levodopa and have modified the abstract, motor section as well as the conclusion accordingly. In particular, we have now also advised to take dopamine agonists and levodopa into consideration in those patients who need immediate and robust control of their motor symptoms from the beginning.

The authors already mentioned originally that dopamine agonists are less likely to cause motor complications in comparison to levodopa and that this is not exclusive to MAO-B inhibitors, but now point that out a little more explicitly.

In line with the acknowledged inferiority of MAO-B inhibitors, the authors have replaced the terms “sufficient” and “control” accordingly.

- Section 2:
The revised manuscript now covers previous controversies about the safety of combined treatment with levodopa and selegiline (Lees et al., 1995), which seemed to affect particular patient groups.

- Section 3:
The authors acknowledge the presence of parenteral forms of dopamine agonists, which may be used for those patients who experience swallowing difficulty or just wish to have a different form of drug delivery, e.g. transdermal rotigotine. These alternatives have been explicitly mentioned in conjunction with our discussion on orally disintegrating selegiline.

- Section 4:
As recommended by the reviewer, the authors have now included a brief summary on preclinical data on neuroprotection with MAO-B inhibitors to further support the argument of putative disease-modifying capabilities in MAO-B inhibitors.

We have furthermore mentioned that neuroprotective properties were also claimed for levodopa (ELLDOPA trial) and dopamine agonists (REAL-PET, CALM-PD),
although the interpretation of these trials is hampered by various methodological difficulties.

We hope that our revision has helped to improve our manuscript substantially and that the revised manuscript is now acceptable for publication in BMC Neurology.

Best wishes,

Matthias Loehle, MD