Reviewer’s report

Title: Controversies in Neurology: why monoamine oxidase B inhibitors could be the best choice for initial treatment of Parkinson’s Disease

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Reviewer: Laszlo Vecsei

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This is an excellent overview of the current literature of MAO B inhibitors in terms of clinical use. The major issue is the lack of reliable clinical trials to compare head to head the different clinical modalities (i.e. selegiline vs rasagiline, MAO-B inhibitors vs dopamine agonists, etc.) However, in the everyday clinical practice the physicians need clear recommendation for therapeutic options, and I believe this review definitely meets this expectation.

One can fully agree with the authors that the treatment can be initiated with MAO B inhibitors in early stage of the disease. However, the evidence supported this idea, are not too strong. The clinical efficacy of these drugs is not too robust, meaning that they can not be used for long period, as monotherapy. In DATATOP and in ADAGIO studies the average improvement was 1-2 point in the UPDRS motor scale, which can be neglected in clinical practice. Also the side effects can be significant (confusion, agitation and even hallucinations), especially in elderly, which limit their use. Regarding the disease modifying effect, it is very hard to prove in human. This hypothesis is based on the ADAGIO study only, which is probably the best design to demonstrate any modifying effect. However, in the light of ELLDOPA trial, this effect can be questioned. The authors should also deal with these issues the manuscript.

Other problem, which also affects this research area and is not mentioned, the lack of head to head comprehension of different MAO B inhibitors. Such a trial will not be likely to conduct in the near future. 

Overall, this is a fascinating issue, when the term disease modification enters into the treatment of Parkinson’s disease, however further studies needed to find the exact role of MAO B inhibitions in the therapeutic algorithm. This review is an excellent one to draw the attention of these concerns.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a
statistician.

Declaration of competing interests:

I declare that I have no competing interests.