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: Oren S Cohen

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In this review Lohle and Reichmann tries to prove that MAO-B inhibitors are the best choice for initial treatment of Parkinson's disease. They base their claim on four major arguments:

1. MAO-B inhibitors provides sufficient symptomatic control for early PD.
2. MAO-B inhibitors are well tolerated.
3. MAO-B inhibitors are easy to use.
4. MAO-B inhibitors potentially have a disease modifying effect.

The introduction is well written. The need for an early treatment and the purpose of the manuscript are well clarified.

Section 1.

-The effect of MAO-B inhibitors is only mild (DATATOP, TEMPO) and is defiantly inferior to of dopamine agonists (DA) (Barone et al, Neurology 1999;53:573-9). Some may even argue whether an effect of 3 point in the total UPDRS or less than 2 points in the UPDRS III could be defined as a clinically significant effect (Scrag et al, Mov Dis 2006;21:1200-7). More than that in contrary to DA in which monotherapy is possible in 20% of the patients for up to 5 years (Parkinson study group JAMA 2000:1931-8) it was shown that patients receiving monotherapy with MAO-B inhibitors were more likely to require add on therapy during follow up than those receiving levodopa or DA. (Caslake et al. Cochrane Database sys rev 2009)

All this suggests that in terms of efficacy MAO-B inhibitors are inferior to DA for initial treatment and I believe this should be discussed in the section.

- Delaying the time to the development of dyskinesia is not unique to MAO-B inhibitors and was reported for DA as well (Stowe et al. Cochrane Database sys rev 2008) (actually it may be an effect of the early treatment.)

- In the view of the mild symptomatic effect of the MAO-B inhibitors the terms "sufficient" and "control" are inappropriate and should be changed (Minor Essential Revision).
Section 2.
- There is no doubt MAO-B inhibitors have a better safety profile compared to DA. However, in my view, the controversy concerning worse survival with selegiline worth mentioning (Less et al. BMJ 1995;311:1602-5, Berteler et al. BMJ 1998;316:1182-3) (Discretionary Revision)

Section 3.
- The authors argue that MAO-B inhibitors are easy to use since they are taken once or twice daily and since they have disintegrating formulations that can be taken in patients with dysphagia. However since most DA marketed today has long acting -once daily formulations, MAO-B inhibitors have no advantage in this aspect. -Concerning the dysphagia we know that this symptom is very rare in early PD (and if present early in the disease course another diagnosis like MSA should be considered). More than that DA also have parenteral formulation (Rotigotine patches and Apomorphine pumps) that are available for use in patients with dysphagia. (Minor Essential Revision).

Section 4.
- In order to further support their claim on the potential neuroprotective effect of MAO-B inhibitors the authors may consider adding some data from preclinical (in vivo and in vitro) studies showing such an effect (Discretionary Revision)

- In addition it should be mentioned that studies with DA (CALM-PD and REAL-PET) also suggest a potential neuroprotective effect (Discretionary Revision)

- Although the review is well written, I believe it should be written in a more objective manner, comparing the MAO-B inhibitors with other treatment options (e.g. DA) mentioning the relative advantages (safety profile, neuroprotection) and disadvantages (relatively low efficacy) of those medications (Major Compulsory Revision).