Monoamine oxidase type B inhibitors in early Parkinson’s disease: meta-analysis of 17 randomized trials involving 3525 patients
BMJ 2004;329:593-600 (August 13)

Study Type: Meta-analysis
Purpose: Meta-analysis of data from randomized trials comparing MAOBI’s with either levodopa or placebo in early PD.
Patients: 3525 patients; 17 trials
Meta-analysis design: Studies were identified through Medline, Cochrane, Embase, Pubmed, conference proceedings, and abstracts, quality of the trials were assessed by specific criteria
Inclusion: randomized controlled trials from 1966 to 2003, early PD treatment, could be given with or without levodopa versus placebo, trial duration of 6 weeks to 10 years
Exclusion: 18 trials - one trial excluded
Drug: Selegiline (13 trials), lazabemide (3 trials), rasagiline (1 trial)
Outcomes: All-cause mortality, disability scales, need for levodopa, incidence of minor complications, side effects

1. Is the meta-analysis valid?
   Primary Guides
   a. Did the overview address a focused clinical question? yes
   b. Were the criteria used to select articles for inclusion appropriate? yes
   Secondary Guides
   a. Is it unlikely that important, relevant studies were missed? yes
   b. Was the validity of the included studies appraised? yes
   c. Were the assessments of studies reproducible? yes
   d. Were the results similar from study to study? yes

2. What were the results?

<table>
<thead>
<tr>
<th>ACE Inhibitor vs placebo</th>
<th>#trials</th>
<th>MAOBI</th>
<th>placebo</th>
<th>p-value</th>
<th>test for</th>
<th>ARR</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause mortality</td>
<td>9</td>
<td>15.5%</td>
<td>18.2%</td>
<td>NS</td>
<td>0.8</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>UK-PDRG</td>
<td>1</td>
<td>28%</td>
<td>18%</td>
<td>.015</td>
<td>---</td>
<td>10%</td>
<td>10</td>
</tr>
<tr>
<td>All trials</td>
<td>10</td>
<td>20%</td>
<td>21%</td>
<td>NS</td>
<td>0.6</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Need for levodopa</td>
<td>8</td>
<td>35.4%</td>
<td>50.7%</td>
<td>.0001</td>
<td>0.2</td>
<td>15.3%</td>
<td>7</td>
</tr>
<tr>
<td>Motor complications</td>
<td>5</td>
<td>38.1%</td>
<td>43.2%</td>
<td>.02</td>
<td>0.3</td>
<td>5.1%</td>
<td>20</td>
</tr>
<tr>
<td>Dyskinesia</td>
<td>3</td>
<td>40.1%</td>
<td>40.3%</td>
<td>NS</td>
<td>0.3</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Withdrawal due to side effects</td>
<td>9</td>
<td>10.3%</td>
<td>5.1%</td>
<td>.04</td>
<td>.09</td>
<td>5.2%</td>
<td>19</td>
</tr>
</tbody>
</table>

3. Will the results help me?
   * The UK-PDRG trial reported an increase in mortality when using selegiline in 1995. The other reported trials do NOT support this finding.
   * Early use of selegiline reduces the need for levodopa.
   * When selegiline is given with levodopa, lower doses of the levodopa are needed.
   * Fewer patients on selegiline develop motor complications.
   * There is no benefit of selegiline over placebo for dyskinesia.
   * There are a lack of comparative trials using selegiline.

Conclusion: For every 100 patients you use selegiline for the treatment of early PD, there would be no effect on mortality in either direction. Over several years, 7 patients would delay their need for levodopa and 20 fewer patients would develop motor complications. In this same 100 patients, 19 would quit using the drug based on side effects (specific side effects were not mentioned).

Author editorial: The hope for Selegiline use in early PD has always been about delaying the progress of the disease or neuroprotection. This meta-analysis does not address this issue and it remains controversial. This MA adds to the literature because it assure us that only one trial has shown an increase in death due to the drug and that was the UK-PDRG (NNH for death was 10 over 6 years).