Donepezil was safe and effective in Alzheimer disease


Main outcome measures
Cognition (Alzheimer’s Disease Assessment Scale—Cognitive Subscale [ADAS-Cog]), global function (Clinician’s Interview-Based Impression of Change scale [CIBIC Plus], which included information supplied by caregiver), and adverse events (i.e., treatment-emergent signs and symptoms). Secondary outcome measures included MMSE scores.

Main results
Analysis was by intention to treat. Patients allocated to donepezil, 5 mg and 10 mg, had greater improvement in their ADAS-Cog scores at 12 weeks than did patients allocated to placebo (mean score change after adjustment for baseline severity −2.1 for 5-mg donepezil and −2.7 for 10-mg donepezil vs 0.4 for placebo; P < 0.001 for both comparisons). Patients allocated to donepezil showed greater improvement in global function (i.e., lower CIBIC Plus scores) at 12 weeks than did those allocated to placebo (mean CIBIC Plus score 3.9 for 5-mg donepezil and 3.8 for 10-mg donepezil vs 4.2 for placebo; P < 0.01 for both comparisons).

Donepezil, 10 mg, vs placebo at 12 weeks in Alzheimer disease*

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Donepezil</th>
<th>Placebo</th>
<th>RRI (95% CI)</th>
<th>NNH (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>22%</td>
<td>8%</td>
<td>174% (50 to 408)</td>
<td>8 (5 to 17)</td>
</tr>
<tr>
<td>Insomnia</td>
<td>18%</td>
<td>5%</td>
<td>239% (64 to 612)</td>
<td>9 (6 to 18)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>13%</td>
<td>3%</td>
<td>408% (88 to 1294)</td>
<td>10 (6 to 20)</td>
</tr>
</tbody>
</table>

*Abbreviations defined in Glossary; RRI, NNH, and CI calculated from data in article.

Commentary (continued from page 178) and not nearly as dramatic as the benefits of dopaminergic agents in Parkinson disease. The scales used in research to detect improvement are difficult to apply clinically.

In practice, for patients and families who are interested in treatment for cognitive deficits, I recommend starting with a careful assessment of function and selection of a few focused outcomes (including general well-being) that are important to the family and patient. Start with a low dose of donepezil, 5 mg/d, for 1 month to look for side effects and assess benefits in the preselected areas. If no side effects or improvement occurs, a dose of 10 mg/d can be tried. For patients who improve at either dose, it is worthwhile to continue the medication. For patients with substantial side effects or no improvement, treatment with the drug can be stopped because it does not apparently affect the long-term course of the disease. Long-term safety is unknown.

On the basis of current research, I urge clinicians to be cautious in describing the expected benefits of cholinergic treatments. The experience of Alzheimer disease can be devastating for some patients and families and may make them particularly vulnerable to unrealistic expectations, including the mistaken belief that a "magic bullet" exists for the disease.

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References
2. Manning A. Treatment for dementia leads mental disorder research. USA Today. 1998 June 10; Section D:7.