Review: galantamine improves most outcomes in suspected Alzheimer’s disease


**QUESTION:** In elderly people with suspected Alzheimer’s disease (AD), does galantamine improve clinical global ratings, cognition, behaviour, and activities of daily living?

**Data sources**
Studies were identified by searching with the terms galantamine and galanthamine in 14 databases and trial registers. The manufacturer of galantamine (Janssen) was also contacted.

**Study selection**
Randomised, unconfounded, blinded, placebo controlled trials were selected if participants were elderly people with suspected AD, if oral galantamine was studied, and if outcomes were assessed using standardised measurement tools (Clinician’s Interview Based Impression of Change plus Caregiver Input [CIBIC-plus], Alzheimer’s Disease Assessment Scale Cognitive Subscale [ADAS-cog], Alzheimer’s Disease Cooperative Study Activities of Daily Living [ADCS-ADL] scale, Disability Assessment for Dementia [DAD] scale, and Neuropsychiatric Inventory [NPI]).

**Data extraction**
Data were extracted on study quality, patient characteristics, drug dosage and duration, and outcomes.

**Main results**
6 trials met the inclusion criteria and had data suitable for analysis. 6 trials evaluated CIBIC-plus. At 6 months, galantamine in doses of 16, 24, and 32 mg/day showed improvements (table) but 8 mg/day did not. All 3 trials evaluating ADAS-cog showed improvements of > 4 points at 6 months with galantamine at doses 16, 24, and 32 mg/day (table) but not at 8 mg/day. 1 trial each evaluated ADCS-ADL and NPI scores: each showed improvements with galantamine, 16 and 24 mg/day but not 8 mg/day.

**Conclusion**
In patients with suspected Alzheimer’s disease, galantamine, in doses between 16 and 32 mg/day improves global clinical status, cognition, activities of daily living, and behaviour but also causes more adverse events than placebo.

**Galantamine (Gala) vs placebo for suspected Alzheimer’s disease**

<table>
<thead>
<tr>
<th>Scales assessed at 6 months</th>
<th>Gala dose</th>
<th>Gala Placebo</th>
<th>RBI (95% CI)</th>
<th>NNT (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CIBIC-plus</td>
<td>16 mg/day</td>
<td>68%</td>
<td>48%</td>
<td>42% (21 to 67)</td>
</tr>
<tr>
<td></td>
<td>24 mg/day</td>
<td>71%†</td>
<td>50%†</td>
<td>32% (20 to 47)</td>
</tr>
<tr>
<td></td>
<td>32 mg/day</td>
<td>51%†</td>
<td>37%†</td>
<td>35% (19 to 54)</td>
</tr>
<tr>
<td>ADAS-cog</td>
<td>16 mg/day</td>
<td>36%</td>
<td>25%</td>
<td>62% (32 to 151)</td>
</tr>
<tr>
<td></td>
<td>24 mg/day</td>
<td>34%†</td>
<td>18%†</td>
<td>52% (18 to 82)</td>
</tr>
<tr>
<td></td>
<td>32 mg/day</td>
<td>35%</td>
<td>15%</td>
<td>129% (52 to 248)</td>
</tr>
</tbody>
</table>

*CIBIC-plus=Clinician’s Interview Based Impression of Change plus Caregiver input showing no change or improvement; ADAS-cog=Alzheimer’s Disease Assessment Scale-Cognitive Subscale >4 points improvement. Other abbreviations defined in glossary; RBI, NNT, and CI calculated from data in article.†Weighted event rates (>1 study).

**COMMENTARY**
The meta-analysis by Olin and Schneider shows that galantamine has similar efficacy to tacrine, donepezil, and rivastigmine, the 3 acetylcholinesterase inhibitors (AChE-Is) currently marketed in the US for treatment of AD. Their comparable efficacy indicates that touted unique properties, such as the allosteric modulation of nicotinic receptors with galantamine, confer no measurable added benefit. Clinicians, therefore, should select an AChE-I based on adverse effect profile, patient tolerance, convenience of dosing, and cost. Although anecdotal reports show clinical improvement after switching non-responders to a different AChE-I, no published data support this practice.

Functional dependency and behavioural disturbances, more than memory loss, contribute to caregiver stress and institutionalisation. Because of the uncertain clinical relevance of the ADAS-cog, recent clinical trials of AD treatments have incorporated instruments to assess their effect on activities of daily living and behavioural complications.1, 2 The slowing of decline in activities of daily living by galantamine and other AChE-Is, as well as these agents’ potential to mitigate behavioural disturbances, represent important reasons to recommend them for patients with AD. Although the major clinical trials have not included patients with advanced AD, long term, open label studies suggest that AChE-Is may delay institutionalisation.3

Calvin H Hirsch, MD
University of California at Davis
Sacramento, California, USA