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Three-Year Outcome of Rivastigmine Treatment in Alzheimer’s Disease in a Routine Clinical Setting

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Conclusions
Long-term rivastigmine treatment in AD yielded positive cognitive, global and functional outcomes in a routine clinical setting. Completers of the 3-year study tolerated higher doses of rivastigmine better than did the patients who dropped out from the study.

Background and objectives
Alzheimer’s disease (AD) is the most common diagnosis among the dementia disorders. AD is characterized by a progressive decline in cognitive and practical abilities and leads to major difficulties in the management of daily life after only a few years of illness. Currently, the main therapy used for mild-to-moderate AD is cholinesterase inhibitor (ChE) treatment, which may delay disease progression. Long-term, placebo-controlled studies of ChEs in AD are not permitted for ethical reasons. Therefore, the advancement of knowledge on longitudinal outcomes in different domains warrants well-designed naturalistic studies. The aim of this study was to explore the 3-year effectiveness of rivastigmine treatment.

Methods
The Swedish Alzheimer Treatment Study (SATS) is a prospective, open, non-randomized and multicentre study for evaluating ChE therapy in clinical practice. In total, 269 outpatients with a clinical diagnosis of AD received rivastigmine. Patients were assessed using cognitive tests (MMSE and ADAS-cog), global performance (CIBIC) and instrumental ADL (IADL) at baseline, after 2 months (MMSE and CIBIC only) and every 6 months, for a total period of 3 years. The 2-year outcomes of this study have been published previously (1). The outcomes were compared with mathematical models of change in ADAS-cog (2) and IADL scores (3, 4) in untreated patients with AD. These models take into consideration the rivastigmine-treated SATS patient scores at baseline. The rates of change were calculated for each individual and illustrated in the figures. The expected decline in MMSE score based on earlier reported untreated historical patients with AD was estimated at 2.4 points/year (5, 6). Three groups of response were defined at each CIBIC interval: 1–3 indicated improvement, 4 indicated no change and 5–7 indicated worsening.

Table 1. Baseline characteristics

<table>
<thead>
<tr>
<th>Number of patients</th>
<th>269</th>
</tr>
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<tbody>
<tr>
<td>Sex (males/females)</td>
<td>48/52%</td>
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<tr>
<td>Estimated age at onset, years</td>
<td>71.1 ± 8.0</td>
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<tr>
<td>Age at the start of rivastigmine treatment, years</td>
<td>74.0 ± 7.7</td>
</tr>
<tr>
<td>Duration of AD years</td>
<td>2.3 ± 2.2</td>
</tr>
<tr>
<td>Education, years</td>
<td>9.4 ± 2.5</td>
</tr>
<tr>
<td>MMSE score, mean change (95% CI) from baseline</td>
<td>23.3 ± 4.3</td>
</tr>
<tr>
<td>ADAS-cog score, mean change (95% CI) from baseline</td>
<td>18.1 ± 8.8</td>
</tr>
<tr>
<td>IADL score, mean change (95% CI) from baseline</td>
<td>14.8 ± 5.2</td>
</tr>
</tbody>
</table>

*mean ± standard deviation (SD)

ADAS-cog, Alzheimer’s Disease Assessment Scale-cognitive subscale; IADL, Instrumental Activities of Daily Living; MMSE, Mini-Mental State Examination

Results
The mean ± SD dose of rivastigmine was 6.2 ± 2.1 mg per day during the study. Three-year completers (n = 117, 44%) received higher mean doses than did drop-outs (7.2 ± 1.9 vs 5.5 ± 2.0 mg/day, p < 0.001).

Figure 1.

MMSE, mean change (95% CI) from baseline

The mean change in MMSE score from the baseline remained above the baseline level for 6 months. After 3 years of rivastigmine treatment, the mean decline of MMSE score from the baseline was 2.8 points (95% CI, 2.1–3.6) (shaded area, 2–4 points/year: expected decline in untreated AD patients).

Figure 2.

ADAS-cog, mean change (95% CI) from baseline

The mean change in ADAS-cog score after 3 years of rivastigmine treatment was 5.7 points (95% CI, 3.7–7.7), which was significantly better than the score predicted by the Stern equation (Figure 2). SATS patients remained untreated (13.1 points; 95% CI, 11.9–14.2, p < 0.001).

Figure 3.

CIBIC

Among the completers, 26% of patients exhibited global improvement or no changes after 3 years of rivastigmine treatment.

Figure 4.

IADL, mean change (95% CI) from baseline

The mean change in IADL score after 3 years of rivastigmine treatment was 6.2 points (95% CI, 5.2–7.2), which was significantly better than the score predicted by the Green equation (Figure 4). SATS patients remained untreated (17.6 points; 95% CI, 16.7–18.5, p < 0.001).

References:

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