Duloxetine vs. Placebo in the Treatment of Elderly Patients with Major Depressive Disorder

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ABSTRACT

Background: Major depressive disorder (MDD) is a common disorder in the elderly and is often associated with physical disability and high mortality rate (Tschanz et al., 2000). The elderly are more susceptible to depression because of economic, physical, and social isolation (Cassidy 2001). In elderly patients with MDD, the presence of comorbid depression is more frequent than in the general population (Rothschild, 1996). Therefore, an antidepressant for elderly MDD patients should not worsen their cognitive functions. Furthermore, it would be considered advantageous if an antidepressant improved cognitive functions in depressive elderly patients.

Objectives: These studies were designed to assess the effects of duloxetine (60 mg QD) on cognitive functions in elderly patients with MDD who met the treatment criteria for MDD while enrolled in a double-blind, placebo-controlled, 8-week trial or were randomized to duloxetine or placebo for the 8-week double-blind phase of a 12-week trial. The objective was to determine whether Duloxetine improved cognition and depression, and was safe and well-tolerated in elderly MDD patients. We also analyzed the impact of treatment with investigator, gender, age, and baseline HAMD 17 on cognitive function.

Methods:

- **Study Design**: Double-blind, placebo-controlled, multicenter randomized trial of 111 elderly MDD patients. After a 1-week screening phase and a 1-week placebo run-in, 111 patients began double-blind treatment at an initial dose of study drug they were assigned.
- **Primary Outcome Measure**: The primary outcome measure was a prespecified composite cognitive score based on four cognitive tests that measured verbal learning and memory, attention, executive functions, and psychomotor speed.
- **Statistical Analysis**: Two-way ANOVA for repeated measures with treatment and visit as factors and investigator, gender, age, and baseline HAMD 17 as covariates.

Results:

- **Primary Outcome Measure**:
  - **Change from Baseline to Endpoint**: The primary outcome measure improved in both treatment groups, with a greater improvement in the duloxetine group compared to placebo (0.56 vs. 0.05, p = 0.001 vs. placebo).
  - **Interactions**: The interaction of treatment with investigator, gender, age, and baseline HAMD 17 was evaluated, but no significant interactions were observed.

Conclusions:

- Duloxetine improved cognition and depression, and was safe and well-tolerated, in elderly MDD patients.
- Treatment with investigator, gender, age, and baseline HAMD 17 did not significantly impact treatment outcomes.

**Table 1. Baseline Characteristics – Demographics and Psychiatric History**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>n=104</th>
<th>n=207</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>Age (years)</td>
<td>71.62</td>
<td>71.68</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>White</td>
<td>Black</td>
</tr>
<tr>
<td>HAMD 17 (mean ± SD)</td>
<td>23.17 ± 6.97</td>
<td>21.97 ± 3.62</td>
</tr>
</tbody>
</table>

**Table 2. Adverse Events Reported as Reason for Discontinuation**

<table>
<thead>
<tr>
<th>Event</th>
<th>Duloxetine 60 mg QD</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevation in BP</td>
<td>0.89 (1.004)</td>
<td>1.004 (2.5)</td>
</tr>
<tr>
<td>Headache</td>
<td>0.54 (0.97)</td>
<td>0.89 (1.21)</td>
</tr>
<tr>
<td>Nausea</td>
<td>0.55 (0.99)</td>
<td>0.76 (1.10)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>0.55 (0.99)</td>
<td>0.76 (1.10)</td>
</tr>
</tbody>
</table>

**Figure 3. Geriatric Depression Scale and HAMD 17**

**Figure 4. Geriatric Depression Scale**

**Figure 5. HAMD 17 Total Score**

**Figure 6. HAMD 17 Response and Remission at Endpoint**

**Figure 7. VAS for Back Pain Score**

**Figure 8. VAS for Time While Awake Score**

**REFERENCES**


**Figure 1. Composite Cognitive Score**

**Figure 2. Individual Cognitive Tests**

**Figure 3. Geriatric Depression Scale and HAMD 17**

**Figure 4. Geriatric Depression Scale**

**Figure 5. HAMD 17 Total Score**

**Figure 6. HAMD 17 Response and Remission at Endpoint**

**Figure 7. VAS for Back Pain Score**

**Figure 8. VAS for Time While Awake Score**

**CONCLUSIONS**

- Duloxetine improved cognitive functions without evidence of significant improvement in the composite cognitive score for elderly MDD patients.
- Depression and anxiety levels, as measured on the Geriatric Depression Scale (GDS) and Hamilton Depression Rating Scale (HAMD 17), were significantly lower in the duloxetine group compared to placebo, with a greater improvement observed in the duloxetine group (0.56 vs. 0.05, p = 0.001 vs. placebo).
- Duloxetine was safe and well-tolerated in elderly MDD patients, with a similar discontinuation rate due to adverse events for duloxetine and placebo (9.7% vs 8.7%). Significantly more placebo patients experienced elevations in blood pressure, with no significant difference in rates of measured orthostatic hypotension between the two treatment groups.

**Fundings**

Funding provided by Eli Lilly and Company