Efficacy of Duloxetine Versus Combined SSRIs (fluoxetine, paroxetine, escitalopram) and Placebo in the Treatment of Major Depressive Disorder

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ABSTRACT

Objective: Compare the efficacy of duloxetine with an SSRI group (including fluoxetine, paroxetine, escitalopram) and placebo.

Methods: Data were pooled from all studies of patients diagnosed with Major Depressive Disorder (MDD) in which duloxetine and SSRIs had been compared. A randomized, double-blind, fixed dose, 6-week studies of duloxetine (N=1133) vs. SSRI (N=689); Placebo, paroxetine, or escitalopram (N=414). Placebo, paroxetine, and escitalopram (N=207) in 7 studies had 40 mg/day (2 studies); 60 mg/day (1 study); 80 mg/day (4 studies); 120 mg/day (4 studies); SSRI doses were 10 mg/day (escitalopram) and 20 mg/day (fluoxetine and paroxetine).

Results: When considering the efficacy of duloxetine across the studied dose range of 40-120 mg/day, duloxetine was significantly superior to the combined SSRIs (fluoxetine, paroxetine, and escitalopram) on the 17-item Hamilton Depression Rating Scale (HAM-D17) total score (9.16 vs. 12.00; p=0.001). Differential efficacy was observed on some depressive symptoms compared with the SSRI group. In the significant difference on the HAMD-21, total score, score ranged from significantly greater efficacy of duloxetine on HAMD-21, individual items. Specific HAMD-21 items, for which duloxetine was significantly superior to combined SSRIs included work and activities, psychomotor retardation, sexual functioning, and hypochondriasis. Although there were no items for which the combined SSRI group was significantly superior to duloxetine, differences approached significance for middle insomnia (p=0.107) and late insomnia (p=0.060). The advantage of duloxetine over the combined SSRI group approached statistical significance for the general somatic symptoms item (p=0.098).

Conclusions: This analysis of 7 pooled studies comparing duloxetine to the SSRI fluoxetine, paroxetine, and escitalopram showed a statistically significant advantage on the HAMD-21 total score for duloxetine compared with the combined SSRI group. The differential efficacy was driven by greater improvement for duloxetine-treated patients on the specific depressive symptoms of work and activities (anhedonia), psychomotor retardation, sexual functioning, and hypochondriasis.

INTRODUCTION

Although the causality of both major depression and nondepressive may be more efficacious than drugs that inhibit only one type of SSRI1,2,3 it is also possible that differential efficacy may be due to a different response profile in patients of age. An analysis is often required to obtain the statistical strength needed to detect the signal, but clinically meaningless, differences in overall improvement or differences in response patterns between active comparators. We present a pooled analysis of depressive symptom improvement in 7 randomized, placebo-controlled studies which are candidates as are placebo-controlled studies in which duloxetine was administered with the SSRI fluoxetine (2 studies), paroxetine (4 studies), and escitalopram (1 study). This pooled data set represents all currently available data from studies that included both placebo and SSRI comparators.

In addition, it is not clear that diabetes for depression, we are better able to interpret duloxetine versus SSRI results.

METHODS

Patients

Inclusion criteria for MDD: Chronic depression (N=789); HAM-D17 total score 22 (Study 1) and CGI-Score of 4 or more at initial study visit; MDD patients who were not treatment-naive.

Treatments

Patients were randomized to duloxetine (60 mg once-daily; n=1133), paroxetine (10 mg once-daily; n=414), or placebo (8 mg once-daily; n=414) for 6 weeks. Four studies incorporated a baseline double-blind design (Studies 1 and 2). In total 6 weeks, the study was administered in a titration from 20 mg BID (3 days) to 40 mg BID (7 days) and then to 60 mg BID (Studies 5 and 6). In the other 2 studies, duloxetine 120 mg/day was administered in a titration from 40 mg BID BID (3 days) and then to 60 mg BID (Studies 5 and 6). In the other 2 studies, the study was administered in a titration from 20 mg BID (3 days) to 40 mg BID (7 days) and then to 60 mg BID (Studies 5 and 6). In the other 2 studies, patients initiated duloxetine directly at 60 mg/day. Patients were randomized to paroxetine 20 mg/day (Study 6) or 15 mg/day (Study 7) as the initial and fixed dose through the study.

Data from data collection studies with soft active comparator are presented. Studies 6 study were 6 n studies using the same protocol and were pooled (20 mg duloxetine 414 mg, escitalopram 20 mg, and placebo 6 days; 414 mg, escitalopram 20 mg, and placebo 6 days; 414 mg, escitalopram 20 mg, and placebo). (Study 7) as the initial and fixed dose through the study.

Analyzed:

This was a post hoc analysis.

Data were pooled as recommended in Literature et al.4

Comparisons of Mean Change in HAMD Total Scores and Individual Items

Table: Mean Change in HAMD Total Score (SSRI Comparator Studies)

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients (n=414)</th>
<th>Placebo (n=178)</th>
<th>Duloxetine (n=236)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=414</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 0</td>
<td>-15.37</td>
<td>-13.74</td>
<td>-15.37 (p&lt;0.001)</td>
</tr>
<tr>
<td>Week 1</td>
<td>-15.37</td>
<td>-13.74</td>
<td>-15.37 (p&lt;0.001)</td>
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<tr>
<td>Week 2</td>
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<td>-13.74</td>
<td>-15.37 (p&lt;0.001)</td>
</tr>
<tr>
<td>Week 3</td>
<td>-15.37</td>
<td>-13.74</td>
<td>-15.37 (p&lt;0.001)</td>
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<tr>
<td>Week 4</td>
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<td>-13.74</td>
<td>-15.37 (p&lt;0.001)</td>
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<tr>
<td>Week 5</td>
<td>-15.37</td>
<td>-13.74</td>
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</tr>
<tr>
<td>Week 6</td>
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</tr>
</tbody>
</table>

CONCLUSIONS

While the overall efficacy of duloxetine compared with SSRIs could not be definitively determined due to small sample size, duloxetine did not separate from placebo (N=132 duloxetine 60 mg/d; and N=136 placebo).

The advantage of duloxetine over the combined SSRI group approached statistical significance for the general somatic symptoms item (p=0.098).

Study Limitations

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