A Study of Atomoxetine in Adolescents with ADHD and Major Depressive Disorder
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ABSTRACT

Recent attention has focused on the safety of drugs labeled for the treatment of depression in pediatric patients. Because attention-deficit/hyperactivity disorder (ADHD) may co-occur with depression, we examined the efficacy and safety of atomoxetine, a noradrenergic reuptake inhibitor, in the treatment of ADHD and major depressive disorder (MDD) in adolescents. Patients with ADHD and MDD (n = 135) were randomly assigned to either atomoxetine (ATX; n = 70) and treated for up to 9 weeks. Treatment-emergent adverse events were monitored throughout the trial, and at the end of the trial, patients who had not completed all visits had their CDRS-R scores imputed using an LOCF analysis. At endpoint, all but one patient in the ATX group had YMRS scores <15. At endpoint, the mean change from baseline to endpoint in the ADHD RS total score was -13.3 (SD 10.0) for the ATX group and -5.1 (SD 9.9) for the placebo group (P < .001). The mean final dose was 1.51 ± 0.24 mg/kg/day for patients not requiring an adjustment. All doses were administered once daily. Supported by funding from Eli Lilly and Company.

INTRODUCTION

• Attention-Deficit/Hyperactivity Disorder (ADHD): -Affects 3% to 7% of school-aged children in the United States1 -Characterized by inattention and/or hyperactivity and impulsivity -Implicated by the dysfunction of the neurotransmitter systems involved
• Atomoxetine: -Selective inhibitor of the presynaptic norepinephrine transporter (NET) approved by the FDA for ADHD treatment in children, adolescents, and adults
• ADHD and Comorbid Depression -ADHD and mood disorders are frequently comorbid.2-7
• Study Objective -This study compared atomoxetine with placebo in the treatment of adolescents with ADHD and MDD.

METHODS

• Subjects: Adolescents 12 and <18 years old who met DSM-IV criteria for both ADHD and MDD
• Inclusion Criteria: -Patients with ADHD-RS scores 1.5 standard deviations above age and gender norms -Children/Adolescents Depression Rating Scale (CDRS-R) score ≤40
• Exclusion Criteria: -Patients beginning structured psychotherapy of ADHD and/or depression less than 1 month prior to entry -Recent use of psychostimulants
• Study Design: -Randomized, double-blind, placebo-controlled trial -Patients randomized to approximately 9 weeks of atomoxetine or placebo -The target atomoxetine dose (1.2 mg/kg/day) could be increased to 1.8 mg/kg/day for patients not responding adequately -All daily doses were administered once daily -Vide 1 and 2 were screening and baseline assessment visits followed by a placebo lead-in phase at Visit 3 through 5 -At the beginning of Visit 6, patients began double-blind treatment with placebo or atomoxetine -Endpoints for efficacy analysis were at Visit 6 through 9

RESULTS

• Primary Efficacy Measures -ADHD-RS and CDRS-R Total scores -ADHD scores on the ADHD RS improved significantly in patients in the atomoxetine group. -CDRS-R total scores at endpoint were significantly different between groups. -At the end of the trial, patients who had not completed all visits had their CDRS-R scores imputed using an LOCF analysis.

Patient Demographics

<table>
<thead>
<tr>
<th>Age</th>
<th>Male</th>
<th>Female</th>
<th>Caucasian</th>
<th>Extensive metabolizer</th>
<th>CYP2D6 Genotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>14.6 (1.8)</td>
<td>52 (74.3)</td>
<td>18 (25.7)</td>
<td>64 (92.8)</td>
<td>16 (22.2%)</td>
<td>64 (92.8%)</td>
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CONCLUSIONS

• ADHD scores on the ADHD RS improved significantly in patients in the atomoxetine treatment group.
• Depression scores on the CDRS-R improved for both placebo and atomoxetine treatment groups but the change from baseline was not significantly different between groups.
• The incidence of treatment-emergent mania symptoms was low and not significantly different between groups.
• The incidence of nausea and decreased appetite occurred significantly more frequently in the atomoxetine treatment group compared with the placebo group.
• For adolescent patients with ADHD and MDD, atomoxetine is safe and tolerable, and is effective for symptoms of ADHD. However, there is no evidence of efficacy for MDD.

Supported by funding from Eli Lilly and Company.

References

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