Randomized Placebo-Controlled Trial of Escitalopram and Venlafaxine XR in the Treatment of Generalized Anxiety Disorder

Anjana Bose, Ph.D., Andrew Korotzer, Ph.D., Carl Gommoll, M.S., and Dayong Li, Ph.D.

Generalized anxiety disorder (GAD) is a highly prevalent and disabling condition. Escitalopram and venlafaxine extended release (XR) both are indicated for the treatment of GAD. Outpatients (ages 18–65 years) with DSM-IV-defined GAD (Hamilton Anxiety Scale [HAMA] ≥ 20) were eligible to participate in this randomized, double-blind, placebo-controlled, multicenter, flexible-dose trial. Following randomization, patients received 8 weeks of double-blind treatment with escitalopram (10–20 mg/day; N = 127), venlafaxine XR (75–225 mg/day; N = 129), or placebo (N = 136). The primary efficacy parameter was mean change from baseline at week 8 in HAMA total score, using the Last Observation Carried Forward (LOCF) approach. Secondary efficacy parameters were HAMA psychic anxiety subscale, Clinical Global Impressions of Severity (CGI-S) and Improvement (CGI-I) scales. Treatment was completed by 77% of patients. The least square mean difference for change from baseline at week 8 in HAMA total score for escitalopram and venlafaxine XR versus placebo were −1.52 (P = .09) and −2.27 (P = .01), respectively, for LOCF, and −1.92 (P = .033) and −3.02 (P = .001), respectively, for Observed Cases (OC). On all secondary parameters, both active treatments were significantly superior to placebo on the LOCF and OC analyses. Discontinuation due to adverse events was not different for escitalopram versus placebo (7 versus 5%, P = .61), but was significantly greater for venlafaxine XR (13%) versus placebo (P = .03). Venlafaxine XR, but not escitalopram, separated from placebo on the primary efficacy measure, using the LOCF approach. However, overall efficacy analyses suggest that escitalopram and venlafaxine XR are both effective treatments for GAD. Escitalopram was better tolerated.

Key words: SSRI; SNRI; GAD; efficacy; safety; tolerability

Introduction

Generalized anxiety disorder (GAD) is a highly prevalent, chronic and disabling disorder. Both the National Institute of Mental Health Epidemiologic Catchment Area Project and the National Comorbidity Survey showed lifetime prevalence rates for GAD that exceed 5% [Kessler et al., 1999; Wittchen et al., 1994]. Long-term prognosis is poor, with only 38% of individuals achieving full remission over a 5-year period [Yonkers et al., 2000]. By definition, the symptoms of GAD must significantly interfere with...
functioning to warrant the diagnosis [APA, 2000]. From an economic standpoint, the costs of GAD come mainly from utilization of nonpsychiatric medical treatment and lost productivity [Wittchen, 2002]; the cost of pharmacotherapy for treating GAD is itself a minor contributor to the overall cost of the disease to society [Greenberg et al., 1999].

Serotonin reuptake inhibitors (SRIs) are considered first-line therapy for GAD [Baldwin and Polkinghorn, 2005]. Escitalopram is the most selective of the available SRIs for inhibition of serotonin reuptake [Owens et al., 2001]. There have been four randomized placebo-controlled acute treatment trials of escitalopram in the treatment of GAD, each of which was positive with respect to the prospectively defined primary efficacy outcome, change from baseline to endpoint on the Hamilton Anxiety Scale [HAMA; Baldwin et al., 2006; Goodman et al., 2005]. A placebo-controlled randomized-withdrawal trial has also demonstrated the efficacy of escitalopram in preventing relapse of GAD [Allgulander et al., 2005].

In contrast, venlafaxine inhibits both serotonin and noradrenaline reuptake, particularly at higher therapeutic concentrations [Harvey et al., 2000]. The efficacy of the extended release (XR) formulation of venlafaxine for the treatment of GAD has been established in four positive placebo-controlled acute treatment studies, including two fixed-dose trials of 8-week duration [Davidson et al., 1999; Rickels et al., 2000] and two trials of up to 6-month duration [Allgulander et al., 2001; Gelenberg et al., 2000]. This is the first trial to compare the efficacy and tolerability of escitalopram and venlafaxine XR to placebo in the treatment of GAD.

METHODS

This randomized double-blind placebo-controlled flexible-dose study comparing the efficacy and safety of escitalopram and venlafaxine XR to placebo in the treatment of GAD was conducted at 28 US centers from July 22, 2003 to June 22, 2004.

PATIENT SELECTION

Male and female outpatients (18–65 years) who met DSM-IV criteria for generalized anxiety disorder were eligible for the study. Patients were required to have a minimum total score of 20 on the HAMA [Hamilton, 1959] with a score ≥ 2 on items 1 (anxious mood) and 2 (tension), and a score ≤ 15 on the Hamilton Depression Rating Scale [HAMD; Hamilton, 1960] at screening and baseline. Physical examinations, laboratory tests, and electrocardiograms were required to be normal at screening with any abnormalities judged clinically insignificant. Female patients of childbearing potential were required to have a negative serum β-human chorionic gonadotropin (HCG) pregnancy test and to be practicing a medically accepted form of contraception. Women who were breastfeeding were excluded from the trial.

Patients were excluded from the study if they met DSM-IV criteria for primary diagnoses for any axis I disorder other than GAD as well as patients that met DSM-IV criteria for bipolar disorder, schizophrenia or any psychotic disorder, obsessive compulsive disorder, any personality disorder, mental retardation or any pervasive developmental or cognitive disorder. Patients who met DSM-IV criteria for substance abuse or dependence within the previous 6 months were ineligible to participate, as were those judged to be at risk for suicide. Use of a depot neuroleptic within 6 months before study entry was prohibited, as was the use of any neuroleptic, antidepressant or anxiolytic medication within 2 weeks (or 5 weeks for fluoxetine) before the first administration of double-blind study medication. Patients who had previously been treated with citalopram, escitalopram or venlafaxine XR were not eligible to participate, nor were those who previously had failed to respond to adequate trials of any two SSRIs. Patients also were excluded if they had participated in an investigational study or had received treatment with an investigational drug within 1 month before study entry. Patients who received electroconvulsive therapy within 3 months before study entry were excluded. Concomitant use of any psychotropic drug (or any drug with a psychotropic component) was not allowed, except zolpidem or zaleplon as needed for sleep.

The study protocol was approved by the institutional review boards for the participating centers, and all participants provided written informed consent.

STUDY DESIGN

Patients who met eligibility criteria at the screening visit entered a 1-week single-blind placebo lead-in period. Those who completed the placebo lead-in and continued to meet all eligibility criteria at the baseline visit were randomly assigned to receive 8 weeks of double-blind treatment with escitalopram, venlafaxine XR or placebo. Patients randomized to escitalopram treatment received 10 mg/day for the first week, after which the dosage could be increased to 20 mg/day if clinically indicated. Patients randomly assigned to venlafaxine XR initiated treatment at 75 mg/day for the first week, after which the dosage could be increased at the discretion of the investigator to a maximum of 150 mg/day for week 2 and 225 mg/day for weeks 3–8. Dose could be decreased at any time because of adverse events (AEs). The minimum allowed doses were escitalopram 10 mg/day and venlafaxine 75 mg/day.

At the end of 8 weeks, patients began a 2-week double-blind down-titration period. All patients in the escitalopram treatment group received 10 mg/day throughout the down-titration period. Patients receiving venlafaxine 75 or 150 mg/day received 75 mg/day.
during the down-titration period, whereas those patients receiving 225 mg/day received 150 mg/day during week 1 and 75 mg/day during week 2 of the down-titration period. All study medication was administered as a single daily dose that could be taken in the morning or evening.

ASSESSMENTS

Evaluations were conducted at screening, baseline and at the end of weeks 1, 2, 4, 6 and 8 of double-blind treatment. Efficacy assessments including the HAMA, the Clinical Global Impression of Improvement and Severity (CGI-I and CGI-S) [Guy, 1976] and the Visual Analogue Scale for Overall Pain [Huskinsson, 1974] were carried out at baseline (except for CGI-I) and each subsequent visit except at the end of the down-titration period. Additional assessments included the Hospital Anxiety and Depression Scale [HAD; Zigmond and Snaith, 1983], the Quality of Life Scale [Endicott et al., 1993] and the Sheehan Disability Scale [SDS; Sheehan, 1983], which were administered at baseline and the end of weeks 4 and 8. Depressive symptoms were assessed at baseline and the end of week 8 using the 17-item HAMD.

Safety assessments were conducted at every visit and comprised vital signs, body weight and use of concomitant medication. Monitoring of AEs occurred at every visit after the screening visit and included patient reports in response to a nonleading question and investigator observations. Physical examination, electrocardiogram and laboratory tests were carried out at the screening visit only. A serious AE was defined as any event that was fatal, life threatening, led to hospitalization or prolongation of existing hospitalization, or was associated with significant disability or incapacity, a congenital anomaly or birth defect.

STATISTICAL ANALYSIS

Safety analyses were carried out on the safety population, which included all patients who received at least one dose of double-blind study medication. Efficacy analyses were carried out on the intent-to-treat (ITT) population, which included all patients in the safety population who had at least one post-baseline HAMA assessment. Statistical tests were two-sided hypothesis tests carried out at the 5% level of significance.

The numbers and percentage of patients prematurely discontinued from the study were compared for each of the active treatment groups versus placebo using Fisher's exact test. Comparability in baseline demographic and efficacy parameters was tested using either a two-way analysis of variance additive model with treatment group and study center as factors for continuous variables or a Cochran–Mantel–Haenszal test, controlling for study center, for categorical variables.

The primary efficacy parameter was the change from baseline to week 8 in the HAMA total score. The primary analysis was carried out using the Last Observation Carried Forward (LOCF) approach. Comparisons between each of the active treatment groups (escitalopram or venlafaxine XR) and placebo were carried out using a two-way analysis of covariance (ANCOVA) model with treatment group and study center as factors and baseline HAMA score as a covariate. Secondary efficacy parameters included change from baseline in the HAMA psychic anxiety subscale and the CGI-S scores, and the CGI-I score at endpoint. Additional prospectively defined efficacy parameters were changes from baseline at week 8 in Visual Analogue Scale (VAS) Overall Pain score, HAD Anxiety Subscale score, HAD Depression Subscale score, Quality of Life Scale score, SDS score, HAMD score, HAMA Somatic Subscale score, HAMA Anxiety Item score and HAMA Psychic Item score as well as CGI-I response rate (CGI-I ≤ 2) and HAMA response (≥ 50% reduction from baseline) and remission rates (HAMA ≤ 7). Change from baseline for secondary and additional efficacy parameters was analyzed using the same analysis of covariance model as described for the primary efficacy parameter. For CGI-I, the baseline score of CGI-S was used as a covariate. Remission and response rates were analyzed using logistic regression with treatment group and the respective baseline value as explanatory variable. Per protocol, the Observed Cases (OC) approach was used for supportive analyses.

Assuming an effect size (treatment group difference compared with placebo relative to the pooled standard deviation) of 0.35 on the primary efficacy variable, a sample size of 132 patients in each treatment group was estimated to provide at least 80% power at an α level of 0.05 (two-sided) to detect statistical treatment differences.

RESULTS

PATIENT CHARACTERISTICS

Of 597 patients screened for participation in this study, 404 were randomized to double-blind treatment (Fig. 1). Of the 392 patients who received at least one dose of double-blind medication and were included in the Safety Population, 244 (62.2%) were females, and the mean (±SD) age was 37.6 ± 11.5 years (Table 1). All but seven (1.8%) patients received at least one post-baseline HAMA assessment and were included in the ITT population. For both the Safety and the ITT Populations, there were no statistically or clinically significant baseline imbalances in demographic parameters. Double-blind treatment was completed by 104 (76.5%) placebo-treated patients, 102 (80.3%) escitalopram-treated patients and 96 (74.4%) venlafaxine XR-treated patients. There were no differences between groups in specific reasons for premature discontinuation, with the following exceptions: more venlafaxine XR-treated patients withdrew due to AEs than placebo-treated patients (13.2 versus 5.1%, P = .031); more placebo-treated patients withdrew due
to insufficient therapeutic response than venlafaxine XR-treated patients (4.4 versus 0%, \( P = .030 \)).

There were no between-group differences in the proportion of patients who had previously received treatment for GAD (placebo 31.6%, escitalopram 37.0%, venlafaxine XR 30.2%, \( P = .385 \)). Similar numbers of patients in each treatment group reported a history of nonresponse or intolerance to GAD treatment. Fourteen (10.3%) placebo, 14 (11.0%) escitalopram and nine (7.0%) venlafaxine XR patients had ongoing secondary psychiatric disorders, the most prevalent of which were social phobia and depression.

Baseline values for efficacy parameters revealed a patient sample with moderate-to-severe GAD (Table 2). There was no imbalance with respect to baseline efficacy values, with the exception of baseline CGI-S score, which was significantly different between groups, with the greatest severity in the escitalopram group.

### EFFICACY

For the primary efficacy outcome, change from baseline at week 8 in HAMA total score using the LOCF approach, the least square mean difference for escitalopram and venlafaxine XR versus placebo was \(-1.52 (P = .09)\) and \(-2.27 (P = .01)\), respectively. Using the OC approach, the least square mean difference for change from baseline at week 8 in HAMA total score was \(-1.92 (P = .033)\) and \(-3.02 (P = .001)\), respectively.

The results for active treatment versus placebo on all protocol-defined continuous efficacy outcomes are presented in Figures 2 and 3. Both active treatments demonstrated superiority to placebo in most measures of disease-specific symptomatology and global outcomes, using both LOCF (Fig. 2) and OC (Fig. 3) approaches. In this trial, neither escitalopram nor venlafaxine produced significantly greater HAMA response (\( \geq 50\% \) reduction from baseline) or remission (HAMA \( \leq 7 \)) than placebo (response: 52.8 and 52.0% for escitalopram and venlafaxine, respectively, and 42.2% for placebo; remission: 31.2% for both escitalopram and venlafaxine, 23.7% for placebo; \( P > .05 \) versus placebo, LOCF). However, both active treatment groups had significantly higher CGI-I response rates (CGI-I \( \leq 2 \)) than the placebo treatment group.

**Figure 1. Flow of patients through the trial.**
(escitalopram 60.0%, venlafaxine 65.6%, placebo 45.9%, \(P<.05\), LOCF).

**SAFETY**

The overall mean (±SD) capsules/day was 2.04±0.57 for placebo, 1.85±0.58 for escitalopram and 1.74±0.60 for venlafaxine XR. For active treatment, the overall mean doses were escitalopram 15.7 mg/day and venlafaxine XR 130.0 mg/day. For week 8, the mean (±SD) capsules/day was 2.51±0.66 for placebo, 2.30±0.75 for escitalopram and 2.28±0.74 for venlafaxine XR; for active treatment the mean doses for week 8 were 17.7 mg/day for escitalopram and 171.3 mg/day for venlafaxine XR.

The most commonly reported AEs were ejaculation disorder, nausea, dry mouth, insomnia, somnolence, headache, increased sweating, fatigue and impotence (Table 3). There was no difference in the rate of premature discontinuation due to AEs for escitalopram compared with placebo treatment (7.1 versus 5.1%, \(P=.61\)); significantly more venlafaxine XR patients withdrew for this reason (13.2%, \(P=.03\) versus placebo). One patient who was treated with venlafaxine XR experienced a serious AE, basal cell carcinoma.

Baseline values (mean ± SD mmHg) of systolic and diastolic blood pressure, respectively, were 118.2 ± 12.4 and 75.0 ± 9.5 for placebo, 116.4 ± 13.4 and 75.3 ± 9.3 for escitalopram and 116.6 ± 12.6 and 75.1 ± 9.0 for venlafaxine XR. Following 8 weeks of treatment, mean (±SD mmHg) changes from baseline in systolic blood pressure were -1.41 ± 10.9 for placebo, -0.30 ± 11.15 for escitalopram (\(P=.591\) versus placebo) and 3.67 ± 11.20 for venlafaxine XR (\(P<.001\) versus placebo). Mean (±SD mmHg) changes from baseline to week 8 in diastolic blood pressure were -0.73 ± 8.0 for placebo, -0.05 ± 8.1 for escitalopram (\(P=.405\) versus placebo) and 2.99 ± 7.6 for venlafaxine XR (\(P<.001\) versus placebo). There were no clinically or statistically significant differences in pulse rate or weight.

### TABLE 2. Baseline efficacy values, mean ± SEM, ITT population

<table>
<thead>
<tr>
<th></th>
<th>Placebo (N = 135)</th>
<th>Escitalopram (N = 125)</th>
<th>Venlafaxine XR (N = 125)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAMA total score</td>
<td>23.7 ± 0.3</td>
<td>24.2 ± 0.4</td>
<td>23.8 ± 0.3</td>
</tr>
<tr>
<td>HAMA psychic anxiety subscale</td>
<td>13.6 ± 0.2</td>
<td>13.9 ± 0.2</td>
<td>13.7 ± 0.2</td>
</tr>
<tr>
<td>HAMA somatic anxiety subscale</td>
<td>10.2 ± 0.2</td>
<td>10.3 ± 0.3</td>
<td>10.2 ± 0.3</td>
</tr>
<tr>
<td>HAMA anxiety item</td>
<td>2.75 ± 0.04</td>
<td>2.78 ± 0.04</td>
<td>2.78 ± 0.04</td>
</tr>
<tr>
<td>HAMA psychic item</td>
<td>2.67 ± 0.05</td>
<td>2.76 ± 0.04</td>
<td>2.70 ± 0.04</td>
</tr>
<tr>
<td>HAD anxiety subscale</td>
<td>12.3 ± 0.3</td>
<td>12.8 ± 0.3</td>
<td>12.3 ± 0.3</td>
</tr>
<tr>
<td>HAD depression subscale</td>
<td>7.00 ± 0.34</td>
<td>7.94 ± 0.35</td>
<td>6.97 ± 0.33</td>
</tr>
<tr>
<td>HAMD</td>
<td>11.8 ± 0.2</td>
<td>11.5 ± 0.3</td>
<td>11.4 ± 0.3</td>
</tr>
<tr>
<td>CGI-S*</td>
<td>4.21 ± 0.04</td>
<td>4.35 ± 0.05</td>
<td>4.17 ± 0.04</td>
</tr>
<tr>
<td>VAS</td>
<td>23.5 ± 2.2</td>
<td>25.7 ± 2.4</td>
<td>25.2 ± 2.2</td>
</tr>
<tr>
<td>QOL</td>
<td>49.4 ± 0.8</td>
<td>48.5 ± 0.8</td>
<td>50.2 ± 0.8</td>
</tr>
<tr>
<td>SDS</td>
<td>16.6 ± 0.5</td>
<td>16.7 ± 0.6</td>
<td>15.9 ± 0.5</td>
</tr>
</tbody>
</table>

*Significant between-group difference, \(P=.002\).

HAMA, Hamilton Anxiety Scale; HAD, Hospital Anxiety and Depression Scale; HAMD, Hamilton Depression Rating Scale; CGI-S, Clinical Global Impressions of Severity; VAS, Visual Analogue Scale; QOL, Quality of Life; SDS, Sheehan Disability Scale.

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Figure 2. Least square mean difference with 95% confidence interval for escitalopram versus placebo and for venlafaxine versus placebo, endpoint (Last Observation Carried Forward approach). HAMA, Hamilton Anxiety Scale; HAD, Hospital Anxiety and Depression Scale; HAMD, Hamilton Depression Rating Scale; CGI-S, Clinical Global Impressions of Severity; VAS, Visual Analogue Scale; QOL, Quality of Life; SDS, Sheehan Disability Scale; **VAS, Visual Analogue Scale; **Increase in QOL score is indicative of symptom improvement.
SRIs have become recognized as first-line treatments for GAD [Baldwin and Polkinghorn, 2005]. In general, SRIs are better tolerated and have fewer safety risks than some of their therapeutic predecessors, such as the tricyclic antidepressants [Anderson, 2000]. Benzodiazepines are widely used for this indication as well [Stahl, 2002], but are limited in their ability to alleviate psychic anxiety symptoms such as worry, a key feature of the illness [Hoehn-Saric et al., 1988].

For patients seeking treatment, several therapeutic options exist within the SRI class. In the United States, SRIs that have received approval for the treatment of GAD include escitalopram (the most selective of the available SRIs for the serotonin transporter) and paroxetine and the dual serotonin norepinephrine reuptake inhibitors, venlafaxine XR and duloxetine. However, placebo-controlled comparative trials that inform clinicians of the relative utility of the various SRIs in the treatment of GAD have been limited. For the treatment of major depressive disorder, it was initially reported that venlafaxine (in both its immediate-release and extended-release formulations) might be superior to SRIs selective for serotonin (SSRIs) in producing remission [Thase et al., 2001]. However, subsequent analysis by these authors, in which all available comparative MDD studies were included, have shown that the superiority of venlafaxine is limited to the SSRIs fluoxetine and paroxetine [Thase et al., 2005]. The latter analysis of Thase et al. [2005] included two published trials comparing escitalopram and venlafaxine in depressed patients [Bielski et al., 2004; Montgomery et al., 2004]. Neither trial provided any evidence for the superior efficacy of venlafaxine. Thus, comparison of escitalopram and venlafaxine in GAD patients is of considerable interest.

In this trial, escitalopram failed to separate from placebo with regard to the primary analysis, the mean change from baseline to endpoint in HAMA total score, using the LOCF approach, whereas venlafaxine XR did. However, the results of protocol-defined secondary and supportive analyses, including the OC approach to analyzing the primary efficacy parameter, demonstrated the efficacy of both escitalopram and venlafaxine XR. Overall, these results are consistent with previous findings that venlafaxine may have clinical utility in the treatment of GAD, but further investigations are needed to confirm these observations.

### Figure 3. Least square mean difference with 95% confidence interval for escitalopram versus placebo and for venlafaxine versus placebo, week 8 (Observed Cases). HAMA, Hamilton Anxiety Scale; HAD, Hospital Anxiety and Depression Scale; HAMD, Hamilton Depression Rating Scale; CGI-S, Clinical Global Impressions of Severity; QOL, Quality of Life; SDS, Sheehan Disability Scale; *VAS, Visual Analogue Scale; **Increase in QOL score is indicative of symptom improvement.

### TABLE 3. Adverse events with incidence ≥10% in any treatment group, safety population

<table>
<thead>
<tr>
<th>Event</th>
<th>Placebo (N=136)</th>
<th>Escitalopram (N=127)</th>
<th>Venlafaxine XR (N=129)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ejaculation disorder</td>
<td>0.0%</td>
<td>24.4%</td>
<td>28.8%</td>
</tr>
<tr>
<td>Nausea</td>
<td>8.1%</td>
<td>20.5%</td>
<td>26.4%</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>5.9%</td>
<td>8.7%</td>
<td>18.6%</td>
</tr>
<tr>
<td>Insomnia</td>
<td>13.2%</td>
<td>13.4%</td>
<td>17.8%</td>
</tr>
<tr>
<td>Somnolence</td>
<td>7.4%</td>
<td>10.2%</td>
<td>16.3%</td>
</tr>
<tr>
<td>Headache</td>
<td>15.4%</td>
<td>15.7%</td>
<td>14.7%</td>
</tr>
<tr>
<td>Increased sweating</td>
<td>4.4%</td>
<td>3.9%</td>
<td>10.9%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>3.7%</td>
<td>6.3%</td>
<td>10.9%</td>
</tr>
<tr>
<td>Impotence</td>
<td>0.0%</td>
<td>11.1%</td>
<td>0%</td>
</tr>
</tbody>
</table>

*aIncidence as a percentage of male patients, placebo N=51, escitalopram N=45, venlafaxine XR N=52. *P<.05 versus placebo.

### DISCUSSION

SRIs have become recognized as first-line treatments for GAD [Baldwin and Polkinghorn, 2005]. In general, SRIs are better tolerated and have fewer safety risks than some of their therapeutic predecessors, such as the tricyclic antidepressants [Anderson, 2000]. Benzodiazepines are widely used for this indication as well [Stahl, 2002], but are limited in their ability to alleviate psychic anxiety symptoms such as worry, a key feature of the illness [Hoehn-Saric et al., 1988].

For patients seeking treatment, several therapeutic options exist within the SRI class. In the United States,
with those of four previous positive trials of escitalopram in the acute treatment of GAD [Baldwin and Nair, 2005; Goodman et al., 2005] as well as four positive venlafaxine XR trials in GAD patients [Allgulander et al., 2001; Davidson et al., 1999; Gelenberg et al., 2000; Rickels et al., 2000].

The confidence intervals for the active treatment-placebo differences for both drugs overlapped considerably for the measures presented in Figure 2. This would be expected if the two drugs have similar efficacy for these dosing regimens. In the case of the SDS, venlafaxine was statistically significant different from placebo, but escitalopram was not; however, as with the other efficacy outcomes, the confidence intervals for both drugs overlapped. Notably, this trial was not powered for a direct comparison of the two active agents, and therefore, no firm conclusions can be made concerning the comparative efficacy of these agents.

Earlier comparative trials of these agents in depression provided evidence that escitalopram is better tolerated than venlafaxine XR [Bielski et al., 2004; Montgomery et al., 2004]. Similarly, in this trial, more venlafaxine XR-treated patients discontinued prematurely due to AEs than placebo-treated patients, which was not the case for escitalopram-treated patients. Venlafaxine XR-treated patients also experienced greater mean changes in blood pressure during this study than placebo-treated patients, whereas escitalopram-treated patients did not. Venlafaxine has previously been associated with development of hypertension [Degner et al., 2004; Feighner, 1995; Thase, 1998].

Interpretation of the results of this trial is limited by the exclusion of comorbid primary psychiatric diagnoses, particularly major depressive disorder, which frequently occurs in patients with GAD [Noyes, 2001]. However, SRI trials in GAD patients often exclude primary psychiatric comorbidities, which make this patient sample comparable to many of those reported in the literature.


REFERENCES


