

Research Article

EFFICACY AND TOLERABILITY OF ESCITALOPRAM IN 12- AND 24-WEEK TREATMENT OF SOCIAL ANXIETY DISORDER: RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, FIXED-DOSE STUDY

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Selective serotonin reuptake inhibitors are the pharmacological treatment of choice for the treatment of social anxiety disorder (SAD). The efficacy and tolerability of fixed doses of escitalopram were compared to those of placebo in the long-term treatment of generalised SAD, using paroxetine as an active reference. Patients with a DSM-IV diagnosis of SAD between 18–65 years of age were randomised to 24 weeks of double-blind treatment with placebo (n = 166), 5 mg escitalopram (n = 167), 10 mg escitalopram (n = 167), 20 mg escitalopram (n = 170), or 20 mg paroxetine (n = 169). Based on the primary efficacy parameter, Liebowitz Social Anxiety Scale (LSAS) total score at Week 12 (LOCF), a significantly superior therapeutic effect compared to placebo was seen for 5 and 20 mg escitalopram and for all doses for the OC analyses. Further improvement in LSAS scores was seen at Week 24 (OC and LOCF), with significant superiority over placebo for all doses of escitalopram, and 20 mg escitalopram was significantly superior to 20 mg paroxetine. Response to treatment (assessed by a Clinical Global Impression-Improvement score ≤ 2) was significantly higher for all active treatments than for placebo at Week 12. Clinical relevance was supported by a significant decrease in all the Sheehan disability scores, and the good tolerability of escitalopram treatment. It is concluded that doses of 5–20 mg escitalopram are effective and well tolerated in the short- and long-term treatment of generalised SAD. Depression and Anxiety 19:241–248, 2004. © 2004 Wiley-Liss, Inc.

Key words: CGI-I; enantiomer; Liebowitz Social Anxiety Scale; paroxetine; response; Sheehan Disability Scale; SSRI

INTRODUCTION

Social anxiety disorder (SAD) is characterised by anxiety in situations in which a person fears that he or she may be exposed to the scrutiny of others. As a result, patients with this disorder avoid, or endure with intense anxiety, a variety of social and performance situations.

The lifetime prevalence rates of SAD in community studies range from 2–16% [Magee et al., 1996; Schneier et al., 1992; Wacker et al., 1992]. Patients with SAD typically do not seek treatment until other conditions such as depression, panic disorder, or alcoholism supervene. Thus, far from being the

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exception, co-morbidity is the norm for patients with SAD. Therefore, it is important to consider the presence of other psychiatric disorders when making the diagnosis.

SAD exists as two distinct subtypes: generalised and non-generalised SAD [Kessler et al., 1998]. Generalised SAD, which is the indication of interest in this paper, is a familial, chronic condition, in which patients fear both a range of social and performance situations, whereas the non-generalised form is usually limited to fear of performance situations.

Placebo-controlled, double-blind studies have shown that fluvoxamine [van Vliet et al., 1994], sertraline [Katzelnick et al., 1995], gabapentin [Pande et al., 1999], and paroxetine [Liebowitz et al., 2002] are clinically effective and statistically significantly superior to placebo in treating patients with SAD.

Selective serotonin reuptake inhibitors (SSRIs) are recommended as the initial treatment of SAD [International Consensus Group on Depression and Anxiety, 1998]; and evidence is accruing to support their use as the standard treatment for this disorder, due to their efficacy, tolerability, effectiveness in co-morbid conditions, and lack of drug dependency [Bandelow et al., 2002; van Ameringen et al., 1999].

The SSRI, citalopram, in the dose range of 20–40 mg daily was effective in patients with SAD in a case series and in an open-label study [Bouwer and Stein, 1998; Lepola et al., 1994; Simon et al., 2001]. Citalopram is a racemic mixture and the S-enantiomer, escitalopram, is the most selective SSRI currently available [Owens et al., 2001; Sánchez et al., 2003]. Recently completed studies have demonstrated the efficacy and tolerability of escitalopram in the short- and long-term treatment of major depressive disorder (MDD) and in the short-term treatment of SAD [Burke et al., 2002; Kasper et al., 2002; Lepola et al., 2003; Wade et al., 2002a,b].

In the present study, paroxetine was selected as the reference SSRI because it is registered for use in the treatment of SAD in several countries. A dose of 20 mg/day is the recommended effective dose according to its summary of product characteristics, and this was an effective and safe dose in a placebo-controlled, dose-finding study for patients with SAD [Liebowitz et al., 2002].

We compare the efficacy and tolerability of escitalopram to that of placebo in the short- and long-term treatment of patients with generalised SAD.

METHODS

STUDY DESIGN AND DOSING SCHEDULE

This randomised, placebo-controlled, fixed-dose, active-reference study included 47 centres in 11 countries. It was conducted in accordance with the principles of Good Clinical Practice, the Declaration of Helsinki [1997], and according to the respective

national laws. Local ethics committees approved the study design and eligible patients gave their written informed consent before participating. After screening, patients entered a 1-week, single-blind, placebo lead-in period before being randomised equally to 24 weeks of double-blind treatment with fixed doses of escitalopram (5, 10, or 20 mg/day), paroxetine (20 mg/day), or placebo. Patients who completed double-blind treatment entered a 2-week, single-blind, placebo run-out period. Efficacy and tolerability were assessed at baseline and after 1, 2, 4, 6, 8, 10, 12, 16, 20, 24, 25, and 26 weeks of treatment; tolerability was also assessed 30 days after the last double-blind dose of study product.

PATIENT POPULATION

The selection criteria were chosen to select physically healthy female and male outpatients with a primary diagnosis of generalised SAD according to DSM-IV criteria. At the screening visit, patients between 18–65 years of age were included if they had a total score ≥ 70 on the Liebowitz Social Anxiety Scale (LSAS), demonstrable fear and avoidance traits in at least four social situations, and a score ≥ 5 on one or more of the Sheehan Disability Scale (SDS) subscales [Sheehan et al., 1998].

Patients were excluded if:

- a) they had another Axis I disorder designated the primary diagnosis within the previous 6 months;
- b) they had a MADRS total score ≥ 18 ;
- c) they had a DSM-IV diagnosis of schizophrenia/other psychotic disorder, mania or hypomania or history thereof, or were currently suffering from alcohol or drug abuse, eating disorders, MDD, panic disorders (patients with panic attacks not due to panic disorders could be included), obsessive-compulsive disorders (OCD), body dysmorphic disorder;
- d) they had an Axis II Cluster B diagnosis;
- e) they had learning difficulties or had other cognitive disorder;
- f) the investigator detected a serious risk of suicide or the patient had a score ≥ 5 in the MADRS item 10 (suicidal tendencies);
- g) they had a known lack of therapeutic response to any SSRI;
- h) they had a known hypersensitivity to citalopram or escitalopram or a history of severe drug allergy or hypersensitivity;
- i) they had taken a psychoactive drug (including antidepressants, beta blockers, benzodiazepines, antipsychotics, and psychoactive herbal remedies), monoamine oxidase inhibitors (MAOI), or prophylactic treatment (lithium, valproate, or carbamazepine) within 2 weeks (5 weeks for fluoxetine) before screening, an investigational drug (within 3 months before), or triptans; or

j) they were receiving (or planning to initiate) formal psychotherapy.

EFFICACY ASSESSMENTS

The primary efficacy measure was the mean change from baseline to Week 12 in LSAS total score using the last observation carried forward (LOCF). The LSAS consists of 24 items: 13 describe performance situations and 11 describe social interaction situations [Liebowitz, 1987]. Each of the items is separately rated for fear and avoidance using a 4-point (0–3) categorical scale. All investigators attended co-rating training sessions to standardise the interview and rating techniques.

Secondary efficacy measures included: mean change from baseline to visit in LSAS total score and subscale (fear/anxiety, avoidance) scores; Clinical Global Impression Severity (CGI-S) score per visit and change from baseline to visit; Clinical Global Impression Improvement (CGI-I) score at each visit; proportion of patients who responded to treatment, defined as patients achieving a score of 1 (very much improved) or 2 (much improved) on the CGI-I; change from baseline in SDS work, social life and family life scores.

TOLERABILITY

Tolerability was based on the incidence of adverse events and on the following clinical assessments: vital signs (systolic and diastolic blood pressure and pulse rate), weight, clinical safety laboratory tests (including haematology and biochemistry), and electrocardiograms (ECG). Adverse events were assessed at all visits and the clinical assessments were made at the screening visit, and at Weeks 12 and 24. The 43-item Discontinuation Emergent Signs and Symptoms (DESS) checklist [Rosenbaum et al., 1998], which is a clinician-rated checklist that queries for signs and symptoms associated with discontinuation or interruption of treatment, was also used to assess tolerability. The DESS score was assessed after the open questioning used for capturing adverse events had been completed at Week 24, and 1 and 2 weeks after abrupt drug cessation during the placebo run-out period.

STATISTICAL ANALYSIS

Efficacy analyses were based on the full-analysis set (FAS), which included all randomised patients who had received double-blind study product and had at least one valid post-baseline assessment on the LSAS. Tolerability analyses were based on the all-patients-treated set (APTS), which included all patients who received at least one dose of double-blind study product.

The primary efficacy analysis of the mean change in LSAS total score from baseline to Week 12 was based on the FAS using LOCF. A general linear model for analysis of covariance (ANCOVA), adjusting for

centres and baseline LSAS total score, was applied. Adjustment of *P*-values in multiple testing (pairwise comparison between each of the escitalopram groups and placebo, and between each of the escitalopram groups and paroxetine) was carried out in the primary analysis and, where appropriate, the secondary analysis using Fisher's Protected Least Significance Difference (LSD) Multiple Comparison Procedure. In the secondary analyses, pairwise comparisons were only carried out if the overall *F*-test was significant at the 5% level.

The mean change from baseline to each visit in the LSAS total score and LSAS subscale (fear/anxiety, avoidance) score, CGI-S score, and SDS (family, social, and work) scores were analysed by ANCOVA using the model described for the primary analysis using nominal visits. CGI-I scores were analysed in the same way as the LSAS total score in the primary analysis omitting the baseline term.

Between-group comparisons of the proportion of patients considered to be treatment responders (CGI-I score ≤ 2) were carried out using Fisher's test.

RESULTS

PATIENT BASELINE CHARACTERISTICS

The 839 patients were evenly distributed between the treatment groups (Table 1). There were no clinically relevant differences in patient demographics or baseline values between the five treatment groups. Most patients were Caucasian, and there was an approximately equal ratio of women to men; their mean age was 37 years. The treatment groups did not differ significantly in age of SAD onset or duration of SAD, baseline height, weight, or BMI.

No between-group differences were seen with respect to medical history or physiological variables or for the severity of SAD, as measured by the baseline LSAS and CGI-S scores. Co-morbidity with depressive symptoms was low, as judged from the mean baseline MADRS total score (7.1) and the paucity of patients with a diagnosis of co-morbid depression or dysthymia (Table 1).

WITHDRAWALS FROM THE STUDY

Two hundred forty two patients (29%) withdrew from the study during the 24-week, double-blind period (Table 2), with similar withdrawal rates in all treatment groups; 22% of all patients had withdrawn by Week 12. Withdrawals due to adverse events were lowest in the 5 mg escitalopram group, whereas withdrawals due to lack of effect were highest in the placebo group. Withdrawal of consent and loss to follow-up each accounted for <7% of withdrawals in any treatment group. Because most of the withdrawals occurred in the first 12 weeks of the study (180 of 242, Table 2), the remaining 12 weeks was too long a period

TABLE 1. Baseline patient characteristics

	PBO	ESC 5 mg	ESC 10 mg	ESC 20 mg	PAR 20 mg
Patients treated (APTS)	166	167	167	170	169
Men (%)	81 (49%)	84 (50%)	71 (43%)	80 (47%)	78 (46%)
Age (yr)					
Mean \pm <i>sd</i>	37.0 \pm 11.8	36.3 \pm 10.9	37.2 \pm 11.3	37.0 \pm 10.6	37.4 \pm 11.4
Range	18–65	18–64	18–64	18–62	19–65
Caucasian (%)	100	99.4	98.8	100	98.2
Age of SAD onset (yr)	17.9	17.3	16.9	17.5	17.5
Duration of disorder (yr)	19.2	18.8	20.3	19.5	19.9
Ongoing depression	1	0	0	1	0
Ongoing dysthymia	0	0	1	0	0
LSAS total score	96.0	94.3	92.4	94.0	94.1
CGI-S score	4.8	4.7	4.7	4.8	4.7
SDS work	6.6	7.0	6.9	6.8	7.0
SDS social life	7.3	7.2	6.9	7.3	7.1
SDS family	4.5	4.3	4.1	4.6	4.6
MADRS total score	7.6	6.8	6.8	7.3	7.2

PBO, placebo; ESC, escitalopram; PAR, paroxetine.

TABLE 2. Withdrawals from study by primary reason (APTS) during the 24-week study period

	PBO		ESC 5 mg		ESC 10 mg		ESC 20 mg		PAR 20 mg	
	<i>n</i>	(%)	<i>n</i>	(%)	<i>n</i>	(%)	<i>n</i>	(%)	<i>n</i>	(%)
Patients Treated (APTS)	166		167		167		170		169	
Patients withdrawn (24 weeks)	50	(30.1)	42	(25.1)	56	(33.5)	49	(28.8)	45	(26.6)
Patients withdrawn (12 weeks)	39	(23.5)	29	(17.4)	39	(23.4)	39	(22.9)	34	(20.1)
Primary Reason										
Adverse event(s)	10	(6.0)	8	(4.8)	16	(9.6)	20	(11.8)	23	(13.6)
Lack of efficacy	28	(16.9)	8	(4.8)	15	(9.0)	11	(6.5)	5	(3.0)
Withdrawal of consent	7	(4.2)	9	(5.4)	9	(5.4)	5	(2.9)	4	(2.4)
Lost to follow-up	4	(2.4)	11	(6.6)	6	(3.6)	7	(4.1)	10	(5.9)

PBO, placebo; ESC, escitalopram; PAR, paroxetine.

to carry observations forward, so most of the efficacy analyses are based on observed case (OC) analysis.

EFFICACY RESULTS

Primary efficacy analysis. The 5 and 20 mg doses of escitalopram were significantly ($P < .001$), and the 10 mg dose of escitalopram was borderline significantly ($P = .059$) more effective than placebo, based on the mean change from baseline to Week 12 (LOCF) in the LSAS total score (Table 3). The reference treatment paroxetine was also effective at Week 12.

Secondary efficacy analyses. Table 3 shows that 5 and 20 mg escitalopram were significantly more effective than placebo for all the secondary analyses at Weeks 12 and 24. Ten milligrams escitalopram and paroxetine were significantly more effective than placebo for most of the secondary analyses at Weeks 12 and 24, the exceptions being LSAS avoidance and CGI-I ≤ 2 at Weeks 12 and 24 for 10 mg escitalopram, and SDS family subscale at Week 12 for paroxetine.

Five and 20 mg escitalopram (and paroxetine) from Week 2, and 10 mg escitalopram from Week 4, were significantly more effective than placebo, based on LSAS (Fig. 1). The improvement in the LSAS total score for patients treated with 20 mg escitalopram was significantly superior to that for patients treated with 20 mg paroxetine from Week 16 onwards (Fig. 2). Furthermore, the efficacy of 20 mg escitalopram was significantly superior to 20 mg paroxetine based on CGI-S score (at Week 24), and SDS subscale scores for work (at Week 16), social (at Week 16), and family (at Week 20).

Exploratory analyses of potential covariates showed no treatment-by-centre or treatment-by-baseline interaction effects on the LSAS score. The same was true for treatment interactions with sex, age, and duration of SAD illness.

In the analysis of responders (patients with a CGI-I ≤ 2), all three doses of escitalopram, as well as paroxetine, were significantly superior ($P < .05$) to placebo at Week 12 (OC) (Table 3). At Week 24 (OC), 5 mg escitalopram and paroxetine were significantly superior ($P < .05$) to placebo, as was 20 mg escitalopram ($P < .001$).

TABLE 3. Mean change from baseline to Weeks 12 and 24 in LSAS (FAS; LOCF and OC), SDS scores and response rates (FAS, OC)

	Week	PBO	ESC 5 mg	ESC 10 mg	ESC 20 mg	PAR 20 mg
Patients treated (FAS)		164	166	162	162	166
LSAS total score (LOCF)	12	-29.5	-38.7***	-34.6	-39.8***	-39.3***
LSAS total score (OC)	12	-34.5	-43.1**	-40.4*	-46.1***	-44.2***
	24	-43.4	-51.6**	-50.9*	-60.8***	-53.1**
LSAS avoidance subscale	12	-18.1	-22.0**	-20.9	-23.9***	-22.3**
	24	-22.8	-26.3*	-25.7	-30.8***	-26.7**
LSAS fear/anxiety subscale	12	-16.4	-21.1**	-19.6*	-22.2***	-21.8***
	24	-21.0	-25.3**	-25.0**	-30.0***	-26.2**
SDS work subscale	12	-2.48	-3.58***	-3.29**	-3.79***	-3.41***
	24	-3.12	-4.26***	-4.18***	-5.00***	-4.17***
SDS social subscale	12	-3.00	-3.79**	-3.46	-3.92***	-3.64*
	24	-3.40	-4.54***	-4.59***	-5.29***	-4.38***
SDS family subscale	12	-1.88	-2.34*	-2.33*	-2.37*	-2.23
	24	-2.07	-2.97***	-3.04***	-3.26***	-2.74**
CGI-S	12	-1.35	-1.89***	-1.75**	-1.96***	-1.86***
	24	-1.75	-2.18**	-2.22**	-2.63***	-2.30***
CGI-I ≤2 (responders)	12	50%	69%**	66%*	71%**	72%***
	24	66%	79%*	76%	88%***	80%*

Difference versus placebo: * $P < .05$; ** $P < .01$; *** $P < .001$.
 PBO, placebo; ESC, escitalopram; PAR, paroxetine.

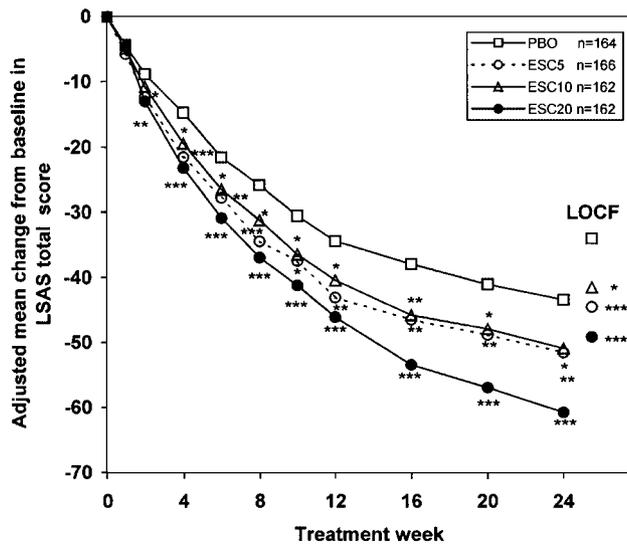


Fig. 1. Adjusted mean change from baseline in LSAS total scores by visit (FAS, OC). Difference versus placebo: * $P < .05$; ** $P < .01$; *** $P < .001$. PBO, placebo; ESC, escitalopram. n = patient numbers (LOCF).

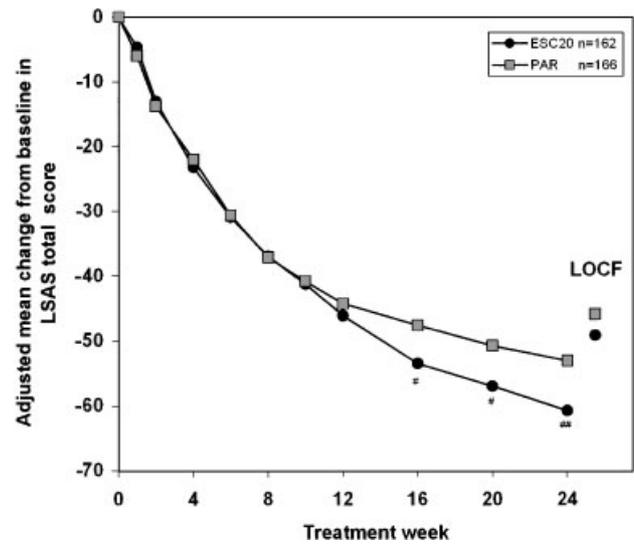


Fig. 2. Adjusted mean difference from baseline in LSAS total scores by visit (FAS, OC). Difference versus paroxetine $P < .05$; $P < .01$. ESC, escitalopram; PAR, paroxetine. n = patient numbers (LOCF).

TOLERABILITY RESULTS

The incidence of treatment-emergent adverse events (TEAE) was similar in the paroxetine and 20 mg escitalopram groups (Table 4). Investigators considered the majority of TEAE to be mild or moderate in all treatment groups. The number of patients who withdrew due to adverse events was similar for the 5 mg escitalopram and placebo groups, and for the

paroxetine and 20 mg escitalopram groups (Table 2). The incidence of constipation in the paroxetine group was five times higher than that in any of the escitalopram groups, whereas the incidence of diarrhoea and yawning in the 20 mg escitalopram group was approximately twice that in any other treatment group. There were no clinically relevant changes in the adverse event profile of any treatment groups from Weeks 12–24.

TABLE 4. Treatment-emergent adverse events at Week 24 with an incidence $\geq 5\%$ and \geq twice that in the placebo group

	PBO		ESC 5 mg		ESC 10 mg		ESC 20 mg		PAR 20 mg	
	<i>n</i>	(%)	<i>n</i>	(%)	<i>n</i>	(%)	<i>n</i>	(%)	<i>n</i>	(%)
Patients treated (APTS)	166		167		167		170		169	
Patients with TEAEs	101	(60.8)	115	(68.9)	121	(72.5)	133	(78.2)	134	(79.3)
Nausea	17	(10.2)	34	(20.4)	33	(19.8)	49	(28.8)	49	(29.0)
Fatigue	15	(9.0)	19	(11.4)	20	(12.0)	24	(14.1)	30	(17.8)
Increased sweating	3	(1.8)	9	(5.4)	18	(10.8)	20	(11.8)	24	(14.2)
Diarrhoea	9	(5.4)	14	(8.4)	9	(5.4)	19	(11.2)	7	(4.1)
Somnolence	4	(2.4)	10	(6.0)	20	(12.0)	19	(11.2)	19	(11.2)
Ejaculation failure [men]	1	(1.2)	1	(1.2)	3	(4.2)	8	(10.0)	8	(10.3)
Dizziness	9	(5.4)	7	(4.2)	10	(6.0)	15	(8.8)	18	(10.7)
Yawning	·	·	2	(1.2)	3	(1.8)	14	(8.2)	6	(3.6)
Libido decreased	2	(1.2)	4	(2.4)	5	(3.0)	11	(6.5)	14	(8.3)
Weight increase	4	(2.4)	10	(6.0)	4	(2.4)	11	(6.5)	11	(6.5)
Anorexia	1	(0.6)	3	(1.8)	9	(5.4)	10	(5.9)	6	(3.6)
Impotence [men]	2	(2.5)	·	·	4	(5.6)	3	(3.8)	4	(5.1)
Constipation	1	(0.6)	2	(1.2)	2	(1.2)	2	(1.2)	10	(5.9)

PBO, placebo; ESC, escitalopram; PAR, paroxetine.

The proportion of patients with a total DESS score ≥ 4 showed a modest and transient increase 1 week after abrupt discontinuation of medication. At the end of the run-out period (Week 26), the proportion of patients with a change from Week 24 in DESS total score ≥ 4 for the 10 and 20 mg escitalopram groups had returned to a level comparable to that before discontinuation.

Analysis of clinical safety laboratory tests, vital signs, BMI, and ECG parameters showed no clinically relevant mean changes from baseline. Escitalopram was well tolerated in the long-term treatment of SAD.

DISCUSSION

PATIENT SAMPLE

The high baseline LSAS total score of > 92 in all of the treatment groups, the baseline CGI-S score of approximately 4.7, and the baseline SDS score between 6.6 and 7.3 (on a 10-point scale) for the work and social life items all indicate that this study population represents markedly ill and socially disabled patients. The high average LSAS total score at baseline indicates a more severely ill patient sample than that reported in other published clinical trials [Kasper et al., 2002; Liebowitz et al., 2002]. For comparison, in Liebowitz et al. [2002], the patients in the 20 mg paroxetine group had a baseline LSAS score of 80.

In the present study, the mean age of onset of the disorder was 17 years and its chronicity was evident from the average duration of the disorder, which was more than 19 years. To investigate the specific efficacy of escitalopram in SAD, a patient population with a low level of co-morbidity was selected, despite the fact that most patients with SAD have significant co-morbidity.

Only two patients had ongoing co-morbid depression and one patient had ongoing dysthymia. The average MADRS total score of 7.1 indicates the absence of significant depressive symptoms. The patients in this study thus represent a population with relatively pure generalised SAD.

WITHDRAWALS

The total withdrawal rate of 22% by Week 12 (29% by Week 24) is lower than that in a comparable fixed-dose study with paroxetine [Liebowitz et al., 2002]. Most of the withdrawals occurred within the first 12 weeks, indicating that escitalopram is suitable for the long-term treatment of SAD. Low and similar withdrawal rates in the treatment groups including the paroxetine reference group justify the use of OC data when analysing efficacy results for a long-term study.

THERAPEUTIC EFFICACY

Due to the above-mentioned withdrawal pattern in this long-term study, the efficacy analyses were primarily based on observed cases (OC). All three doses of escitalopram were significantly more effective than placebo at the end of the 24-week (OC) trial period on both the primary and secondary efficacy parameters. The 20 mg dose of escitalopram was significantly superior to the 20 mg dose of paroxetine ($P < .01$), based on the change from baseline in LSAS mean score (Week 24, OC), and to the other escitalopram doses. The justification for using paroxetine in a dose of 20 mg as the active reference comes from the fixed-dose study by Liebowitz et al. [2002], which showed that 20 mg paroxetine was the optimal dose for the treatment of SAD with no further significant benefit for the 40 and 60 mg dose groups.

The primary analysis in the present study showed a decrease in the total LSAS score of 39.8 points for 20 mg escitalopram and a remarkable decrease of 29.5 points in the placebo group at Week 12 (LOCF). The effect size (decrease in the mean LSAS score from baseline to the primary analysis endpoint) in the escitalopram groups was comparable to that reported in other SSRI studies [Kasper et al., 2002; Liebowitz et al., 2002]. A high placebo response has been reported in other studies of SAD [Kasper et al., 2002].

TOLERABILITY

Because patients with SAD may need a long treatment period, a favourable tolerability profile and a low adverse event withdrawal rate are important in the successful treatment of this chronic disease. Low withdrawal rates due to adverse events (5–12%) show that escitalopram was generally well tolerated. Nausea, a well-known adverse reaction to SSRI treatment, was transient and the most frequently reported adverse event in the active treatment groups; the other adverse events were similar to those reported in depression studies. There were no clinically relevant mean changes observed in clinical safety laboratory tests, ECG values, or vital signs. The further improvement in the LSAS total score from Weeks 12–24, without an additional adverse event burden, demonstrates that long-term treatment with escitalopram is beneficial.

CLINICAL IMPLICATIONS

This study clearly demonstrates that escitalopram is effective in the treatment of social anxiety disorder. The primary efficacy analysis showed 5 mg and 20 mg escitalopram to be statistically significantly superior to placebo based on the mean change in LSAS total score from baseline to Week 12, with borderline statistical significance for 10 mg escitalopram. LSAS total scores (OC) were significantly lower than placebo for 5 and 20 mg doses of escitalopram from Week 2, and for the 10 mg escitalopram dose from Week 4. All three doses of escitalopram were significantly superior to placebo in the majority of the secondary analyses at both Weeks 12 and 24.

These data for escitalopram in the treatment of SAD are robust and clinically relevant, as the CGI severity and improvement scores, and the Sheehan Disability subscale scores all show that escitalopram is superior to placebo for both functional and symptom assessments.

On the basis of this study, 5, 10, and 20 mg escitalopram doses are effective and well tolerated in both the short- and long-term treatment of SAD. The significantly better effect of 20 mg escitalopram than 20 mg paroxetine at Week 24 is, to our knowledge, the first study in anxiety to show the superiority of one SSRI over another.

The efficacy and favourable tolerability of escitalopram over the entire dose range (5–20 mg/day) in both

short- and long-term treatment, including the period after abrupt discontinuation, makes escitalopram a good option for the treatment of patients with generalised SAD.

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