Efficacy and Tolerability of Controlled-Release Paroxetine in the Treatment of Panic Disorder

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Objective: To assess the efficacy and tolerability of controlled-release paroxetine (paroxetine CR) in the treatment of adults with panic disorder.

Method: Paroxetine CR (25–75 mg/day; N = 444) was compared with placebo (N = 445) in patients with DSM-IV panic disorder with or without agoraphobia in 3 identical, double-blind, placebo-controlled, 10-week clinical trials that were pooled for analysis.

Results: Paroxetine CR was statistically superior to placebo in the primary outcome measure, percentage of patients who were free of panic attacks in the 2 weeks prior to endpoint. Of the total population that completed or prematurely terminated treatment, 63% and 53% of paroxetine CR– and placebo-treated patients, respectively, were panic-free during the final 2 weeks ($p < .005$; odds ratio [OR] = 1.63; 95% CI = 1.21 to 2.19). For week 10 completers (72% of total), 73% and 60% of paroxetine CR– and placebo-treated patients, respectively, were panic-free at week 10 ($p < .005$; OR = 2.11; 95% CI = 1.45 to 3.07). Paroxetine CR was also statistically superior to placebo on the global improvement and severity items of the Clinical Global Impressions scale and in reducing anxiety symptoms as measured by the Hamilton Rating Scale for Anxiety total score and total fear and avoidance on the Marks-Sheehan Phobia Scale. Adverse events leading to study withdrawal were minimal and occurred in 11% of the paroxetine CR group and 6% of the placebo group. Most of the treatment-emergent adverse events were rated as mild to moderate in severity and occurred early in the study. There were no unexpected adverse events, and serious adverse events were uncommon (10 [2.3%] of the 444 patients treated with paroxetine CR vs. 8 [1.8%] of the 445 patients treated with placebo).

Conclusion: Paroxetine CR is an effective and well-tolerated treatment for panic disorder. Paroxetine CR is associated with low rates of treatment-emergent anxiety as well as low dropout rates from adverse events.

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The pharmacologic treatment of panic disorder has been significantly advanced during the past 20 years as a result of the development and widespread availability of effective and well-tolerated medications. The selective serotonin reuptake inhibitors (SSRIs) are key examples of such medications that have not only become first-line treatment of panic disorder, but are also effective in the treatment of comorbid depression and other anxiety disorders.[1,2]

Despite the favorable tolerability profile of the SSRIs and other medications used to treat panic disorder, patients are frequently intolerant of medication and stop treatment prematurely.[3–5] In one analysis of pharmacotherapy studies, intolerable side effects were cited as the primary reason for treatment failure in 27% of 190 studies using effective medications.[3]

Among the SSRIs, paroxetine has been shown to be an effective choice for treatment of panic disorder.[6–11] A new, enteric-coated, controlled-release formulation of paroxetine (paroxetine CR) has been developed with the goal of improving the SSRI tolerability profile and lowering dropout rates from adverse events while maintaining the therapeutic benefits of paroxetine in the treatment of depression and anxiety disorders. The enteric coating delays tablet dissolution until the tablet passes into the small intestine, where absorption is slowed by the controlled-release mechanism. This controlled-release technology slows the rate of plasma concentration increase and reduces the magnitude of plasma concentration fluctuations at steady state compared with immediate-release (IR) paroxetine. Both of these properties are drivers of adverse

events.[12] Randomized, controlled studies have shown that paroxetine CR is an effective and well-tolerated treatment for major depressive disorder in a general adult population[13] and in medically ill elderly depressed patients.[14] In both studies, improved tolerability was apparent with paroxetine CR relative to paroxetine IR: significantly lower rates of nausea during the first week of treatment[13] and lower rates of premature study withdrawal from adverse events.[14]

To assess the efficacy and tolerability of paroxetine CR in patients with panic disorder, pooled data from 3 identically designed, randomized, multicenter, placebo-controlled, double-blind, flexible-dose, parallel-group trials were analyzed.

METHOD

Study Design

Patients were enrolled in 1 of 3 randomized, multicenter, placebo-controlled, double-blind, flexible-dose, parallel-group trials of identical design. Following a 2-week, single-blind, placebo run-in phase, eligible patients were randomly assigned to double-blind paroxetine CR or placebo. Patients were evaluated at baseline and at weekly or biweekly intervals during a 10-week treatment phase.

Paroxetine CR–treated patients started treatment at 12.5 mg/day for 1 week, with a forced titration to 25 mg/day for the second week. Thereafter, the dosage was increased in increments of 12.5 mg/day, no more frequently than every week based on clinical response and tolerability, up to the maximum of 75 mg/day. Dosage reductions because of adverse events were allowed after week 2. Patients were withdrawn from the study if treatment was interrupted for more than 2 days during the first week. At week 10, or at the time of early withdrawal, patients entered a 2-week taper phase at the investigator's discretion.

Study Population

Patients were recruited in the United States and Canada. Men and women 18 to 65 years of age who met *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (DSM-IV) criteria for panic disorder with or without agoraphobia were eligible to enter the 10-week treatment phase. In addition, eligible patients must have had at least 2 full panic attacks (i.e., ≥ 4 DSM-IV panic attack symptoms) during the 2-week run-in phase. The protocol was approved by the investigational review boards of all study centers, and all patients signed statements of informed consent.

Patients were not eligible if they had another Axis I disorder as a primary or dominant diagnosis within 6 months prior to screening, had a recent DSM-IV diagnosis of substance abuse or dependence, or posed a current, serious suicidal or homicidal risk. Patients undergoing formal psychotherapy/psychoanalysis or recent electroconvulsive therapy were also excluded, as were patients using psychotropic drugs within 14 days of baseline visit or during the study. Patients underwent urine screening at baseline to detect benzodiazepine use. Patients could not be previously unresponsive to paroxetine treatment for panic disorder.

Efficacy Assessment

The primary efficacy measure was the percentage of patients who were free of full panic attacks for the 2 weeks prior to endpoint. Endpoint was defined as the week 10 assessment for those patients who completed the study or, in the case of early withdrawals, the last valid on-treatment assessment. Secondary efficacy measures were number of full panic attacks per 2 weeks, Clinical Global Impressions-Severity of Illness (CGI-S)[15] score, Hamilton Rating Scale for Anxiety (HAM-A)[16] total score, Marks-Sheehan Phobia Scale (MSPS)[17] total fear and avoidance scores, and percentage of responders on the Clinical Global Impressions-Global Improvement (CGI-I) item. Response was defined on the CGI-I as a score of 1 (very much improved) or 2 (much improved).

Safety Assessment

At each visit, vital signs were measured and patients were asked nonleading questions about adverse effects. Routine laboratory testing (i.e., blood chemistry, hematology, and urinalysis) and physical examinations were conducted at baseline and week 10 or upon early withdrawal.

Statistical Methods

Continuous efficacy measures (i.e., percent reduction in full panic attacks per 2 weeks, HAM-A total score, CGI-S score, and MSPS total fear and avoidance scores) were analyzed using analysis of variance models with treatment, study- and site-by-treatment, and baseline effects. Results were presented as the adjusted means and 95% CIs for the difference between the paroxetine CR and placebo groups. Categorical efficacy parameters (responders based on zero full panic attacks and responders based on CGI-I score) were analyzed using logistic regression models with treatment, study, and site effects. Baseline severity was included as a covariate variable in the analysis of primary efficacy. For each patient, this was determined by baseline values that were less than the baseline median for the population versus greater than or equal to the population median.

The primary efficacy variable was also analyzed using longitudinal data analysis methods. The model contained treatment, study, baseline severity, week, and treatment-by-week interactions. Generalized estimating equations were used for inferences. Analysis of data using such methods allows for the systematic inclusion of correla-

tions among repeated measures in patients. Unstructured correlation was adopted for the analysis.

All comparisons between treatment and placebo were based on 2-sided tests. The effects of interactions (i.e., treatment by covariate) were tested for significance at the 10% level. All other statistical assessments were performed at the 5% level of significance. No adjustment in level of significance was made for comparisons performed at multiple timepoints or multiple endpoints.

Efficacy and safety analyses were carried out on the modified intention-to-treat (ITT) population, defined as all patients who were randomly assigned to treatment, received at least 1 dose of study medication, and had at least 1 postbaseline assessment. Efficacy in the modified ITT population was analyzed using the last-observation-carried-forward (LOCF) and observed cases (OC) datasets. In the LOCF analysis, the last observation on treatment was carried forward to estimate data from missed visits occurring after premature withdrawal from the 10-week study. The OC analysis used only data that were collected at each visit, without estimating missing information.

For each study, a total of 134 assessable patients per treatment group was judged sufficient to detect a difference of 20% in percentage of patients free of full panic attacks during the 2 weeks prior to week 10. A response rate of 50% for patients receiving placebo was assumed. This difference is detectable with a power of 90%, given a significance level of 5% using a 2-sided significance test.

At 1 study site that was involved in 2 of the 3 pooled studies, all paroxetine CR–treated patients responded, whereas none of the patients taking placebo responded. Data from this site for both studies were inconsistent with data from the other study sites, causing a significant treatment-by-center interaction. Because of this, efficacy data from the 38 patients in both studies from this study site were excluded from the statistical analyses to provide the most conservative estimate of efficacy. The demographic and safety data include patients from all sites.

RESULTS

Demographic Characteristics

The true ITT population (i.e., those patients who were randomized and enrolled in the study) from the 3 studies consisted of 910 patients. Data on the true ITT population are not reported herein. The combined modified ITT population (i.e., those patients who were randomized and assessed at least once postbaseline) consisted of 889 patients: 444 patients in the paroxetine CR group and 445 in the placebo group. The patients were predominantly female and white and on average were in their late 30s (Table 1). The mean paroxetine CR dosage for patients who completed the 10-week treatment phase was 50 mg/day, which in terms of oral bioavailability is comparable to the currently recommended target dose of 40 mg/day for paroxetine IR treatment of panic disorder.[1]

Table 1. Demographic Characteristics of Patients With Panic Disorder in the Pooled Dataset of 3 Identical, Double-Blind, Placebo-Controlled Trials Comparing Paroxetine Controlled-Release (CR) and Placebo

Characteristic	Paroxetine CR (N = 444)	Placebo (N = 445)
Gender, N (%) (male)	162 (36.5)	194 (43.6)
Age, mean (SD), y	37.6 (10.22)	37.8 (10.61)
Race, N (%)		
White	380 (85.6)	389 (87.4)
Nonwhite	64 (14.4)	56 (12.6)
Duration of panic disorder, y		
Mean (SD)	9.14 (9.01)	9.49 (9.57)
Median[a]	6	6

[a]Median values reported because of the skewed distribution of this variable.

The number of patients completing week 10 was 311 for paroxetine CR and 328 for placebo (639/889, 72%). The overall rate of withdrawal tended to decrease during the 10-week treatment phase. More patients in the paroxetine CR treatment group withdrew as a result of adverse events than in the placebo group (11% vs. 6%, respectively), whereas more patients withdrew because of lack of efficacy in the placebo group than in the paroxetine CR group (6% vs. 3%, respectively). The combined number of withdrawals because of protocol deviation, loss to follow-up, and other reasons was not appreciably different between the placebo and active treatment groups (13.7% vs. 15.8%, respectively).

Efficacy

The treatment groups were not appreciably different at baseline in panic disorder severity, based on the mean duration of panic disorder (Table 1) or secondary efficacy measures (Table 2). At baseline, CGI-S scores were moderate to marked, with patients experiencing a mean of 10 full panic attacks per 2 weeks (Table 2). Because the baseline panic attack frequency was skewed in distribution, the median better reflects the central tendency of the data; the median panic attack frequency at baseline was 5 per 2 weeks in both groups (Table 2).

Paroxetine CR was statistically superior to placebo on the primary outcome measure, the proportion of patients free of full panic attacks during the 2 weeks prior to endpoint (week 10 LOCF) (Figure 1): 63% and 53% of paroxetine CR– and placebo-treated patients, respectively, were free of panic attacks during their final 2 weeks on treatment ($p < .005$; odds ratio [OR] = 1.63; 95% CI =1.21 to 2.19). At week 10 OC, 73% and 60% of paroxetine CR– and placebo-treated patients, respectively, were panic-free ($p < .005$; OR = 2.11; 95% CI = 1.45 to 3.07). Statistical superiority to placebo was also achieved for paroxetine CR–treated patients who com-

Table 2. Efficacy Measure Ratings for Patients With Panic Disorder in the Pooled Dataset of 3 Identical, Double-Blind, Placebo-Controlled Trials Comparing Paroxetine CR and Placebo

	Baseline		Week 10 OC		Week 10 LOCF	
Efficacy Measure	N	Value	N	Value	N	Value
Free of panic attacks/2 wk prior to endpoint						
Paroxetine CR, %			263	73.0	377	62.6
Placebo, %			296	60.1	395	52.7
p Value (95% CI)				< .005 (1.45 to 3.07)		< .005 (1.21 to 2.19)
No. of full panic attacks/2 wk[a]						
Paroxetine CR						
Mean (SD)	377	10.34 (17.7)	263	1.79 (8.46)	377	2.89 (9.94)
Median (range)		5 (2–262)		0 (0–114)		0 (0–114)
Placebo						
Mean (SD)	395	9.63 (14.18)	296	3.09 (9.29)	395	4.66 (11.76)
Median (range)		5 (1–119)		0 (0–77)		0 (0–108)
CGI-S score						
Paroxetine CR, LS mean[b] ± SE	413	4.32 ± 0.04	276	2.42 ± 0.07	413	2.83 ± 0.06
Placebo, LS mean[b] ± SE	421	4.35 ± 0.04	301	2.94 ± 0.07	421	3.21 ± 0.06
p Value (95% CI)				< .0001 (–0.70 to –0.33)		< .001 (–0.54 to –0.21)
CGI-I score of 1 or 2 (response)						
Paroxetine CR, %			276	79.4	413	63.9
Placebo, %			301	54.5	421	46.3
p Value (95% CI)				< .0001 (2.24 to 4.72)		< .0001 (1.57 to 2.74)
HAM-A total score						
Paroxetine CR, LS mean[b] ± SE	361	20.90 ± 0.40	260	9.77 ± 0.43	361	11.49 ± 0.39
Placebo, LS mean[b] ± SE	384	20.32 ± 0.39	289	12.24 ± 0.41	384	13.72 ± 0.38
p Value (95% CI)				< .0001 (–3.63 to –1.31)		< .0001 (–3.29 to –1.16)
MSPS fear total score						
Paroxetine CR, LS mean[b] ± SE	361	43.8 ± 1.29	260	21.8 ± 1.12	361	24.2 ± 0.98
Placebo, LS mean[b] ± SE	383	42.9 ± 1.15	287	28.2 ± 1.06	383	31.0 ± 0.95
p Value (95% CI)				< .001 (–9.5 to –3.4)		< .0001 (–9.5 to –4.2)
MSPS avoidance total score						
Paroxetine CR, LS mean[b] ± SE	360	15.6 ± 0.49	259	8.3 ± 0.42	360	9.2 ± 0.37
Placebo, LS mean[b] ± SE	382	15.2 ± 0.47	285	10.4 ± 0.40	382	11.3 ± 0.36
p Value (95% CI)				< .001 (–3.2 to –1.0)		< .001 (–3.2 to –1.1)

[a]p Value for comparison between drug and placebo is not reported because of skewed distribution.
[b]At baseline visit, means are reported instead of least-squares (LS) means. LS means correspond to analysis of variance model means adjusted for baseline and study effects.
Abbreviations: CGI-I = Clinical Global Impressions-Global Improvement scale, CGI-S = Clinical Global Impressions-Severity of Illness scale, CR = controlled-release, HAM-A = Hamilton Rating Scale for Anxiety, LOCF = last observation carried forward, MSPS = Marks-Sheehan Phobia Scale, OC = observed cases.

pleted 4 weeks of treatment (week 4 OC), and this effect persisted to week 10 (Figure 1).

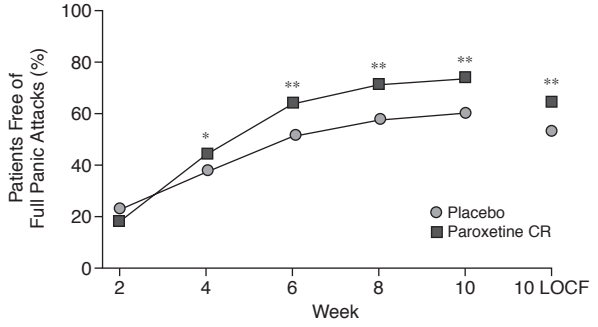
At week 10 LOCF and OC, the mean frequency of full panic attacks in the paroxetine CR–treated group was appreciably less than in the placebo group (Table 2). In fact, a 70.6% versus 54.7% reduction from baseline in number of panic attacks was achieved during the 2 weeks prior to endpoint for the paroxetine CR and placebo groups, respectively ($p = .013$; 95% CI for difference = 3% to 28%) (Figure 2). For the subpopulation that completed treatment, patients treated with paroxetine CR reported an 85.7% reduction in the frequency of panic attacks at week 10 versus 64.0% for placebo ($p = .0006$; 95% CI = 9 to 34).

At endpoint, paroxetine CR was statistically superior to placebo in the proportion of patients with a score of 1 (very much improved) or 2 (much improved) on the CGI-I item (Figure 3) (64% vs. 46%, respectively; $p < .0001$; OR = 2.07; 95% CI = 1.57 to 2.74). At week 10 OC, 79% and 55% of patients in the paroxetine CR and placebo groups, respectively, were CGI-I responders ($p < .0001$; OR = 3.25; 95% CI = 2.24 to 4.72). A statistically significant difference in responder rate was achieved at week 3 and persisted to week 10 (Figure 3).

Paroxetine CR was statistically superior in alleviating general anxiety symptoms, as shown by comparison of HAM-A total scores at week 10 LOCF and OC (Table 2). At week 10, HAM-A total scores in the paroxetine CR group were also significantly less than in the placebo group (LOCF: $p < .0001$, mean difference = –2.23, 95% CI = –3.29 to –1.16; OC: $p < .0001$, mean difference = –2.47, 95% CI = –3.63 to –1.31). Furthermore, the CGI-S item and severity of total fear and avoidance (MSPS), measured at endpoint and week 10 OC, were significantly less in the paroxetine CR group than in the placebo group (Table 2).

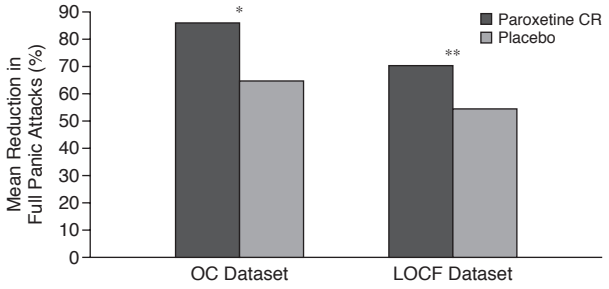
In the analysis of the primary efficacy variable using longitudinal methods, paroxetine CR was significantly better than placebo ($p < .0001$; OR = 2.28; 95% CI = 1.57 to 3.32). A significant quantitative treatment-by-week interaction was observed ($p < .0001$). The fact that the difference between paroxetine CR and placebo was not a constant over time, but continued to increase from week

Figure 1. Percentage of Patients Who Became Free of Full Panic Attacks During the Previous 2 Weeks (week 10 [modified intent-to-treat] LOCF and OC datasets)[a]



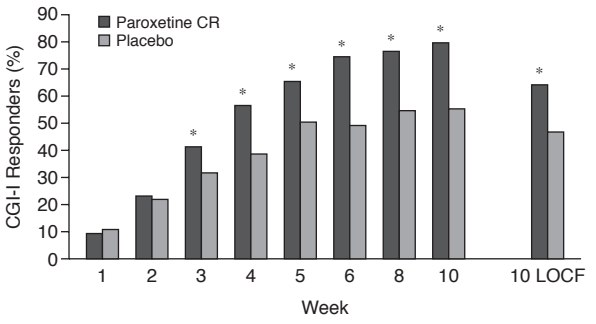
[a]Week 10 LOCF: paroxetine CR, N = 377; placebo, N = 395. Week 10 OC: paroxetine CR, N = 263; placebo, N = 296.
*p < .05.
**p < .005.
Abbreviations: CR = controlled release, LOCF = last observation carried forward, OC = observed cases.

Figure 2. Percentage Reduction From Baseline in Number of Full Panic Attacks per 2 Weeks (week 10 [modified intent-to-treat] LOCF and OC datasets)



*p = .0006; paroxetine CR, N = 263; placebo, N = 296.
**p = .013; paroxetine CR, N = 377; placebo, N = 395.
Abbreviations: CR = controlled-release, LOCF = last observation carried forward, OC = observed cases.

Figure 3. Proportion of Responders (score of 1 or 2) on the CGI-I by Week (week 10 [modified intent-to-treat] LOCF and OC datasets)



*p < .01. Week 10 LOCF: paroxetine CR, N = 413; placebo, N = 421. Week 10 OC: paroxetine CR, N = 276; placebo, N = 301.
Abbreviations: CGI-I = Clinical Global Impressions-Global Improvement, CR = controlled-release, LOCF = last observation carried forward, OC = observed cases.

Table 3. Frequently Reported Adverse Events Occurring in ≥ 5% of Patients (%)

Adverse Event	Paroxetine CR (N = 444)	Placebo (N = 445)
Abnormal ejaculation	27	3
Nausea	23	17
Somnolence	20	9
Insomnia	20	11
Asthenia	15	10
Dry mouth	13	9
Diarrhea	12	9
Impotence	10	1
Nervousness	8	7
Treatment-emergent anxiety	5	4

Abbreviation: CR = controlled release.

2 to week 10, was consistent with the presence of this significant interaction.

The treatment-by-study interaction was not significant in the models presented here. Results from each of the 3 studies supported findings from the pooled analysis. In the first study, the proportion of patients with zero panic attacks at 2 weeks prior to endpoint was significantly greater in the paroxetine CR group versus the placebo group (69% vs. 50%, respectively; p < .004; OR = 2.21; 95% CI = 1.29 to 3.79). Although the second and third studies did not demonstrate a significantly greater proportion of paroxetine CR–treated patients free of panic attacks during the 2 weeks prior to endpoint versus placebo, the second study did demonstrate a significant difference in this measure at week 10 OC (71.3% vs. 56.1%, respectively; p = .012; OR = 2.40; 95% CI = 1.22 to 4.72).

Both of these studies, as well as the first study, showed a significantly greater proportion of responders, as defined by the CGI-I, in the paroxetine CR group versus the placebo group at endpoint (first study: 71.2% vs. 52.9%, respectively; p = .002; OR = 2.30; 95% CI = 1.36 to 3.90; second study: 61.7% vs. 42.0%, respectively; p < .001; OR = 2.31; 95% CI = 1.41 to 3.78; third study: 59.2% vs. 46.3%, respectively; p = .004; OR = 2.17; 95% CI = 1.29 to 3.67).

Tolerability

Paroxetine CR was very well tolerated in this population of patients with panic disorder. Adverse events leading to study withdrawal occurred in 11% of the paroxetine CR group and 6% of the placebo group. Most of the treatment-emergent adverse events were rated as mild to moderate in severity and occurred early in the study. The most frequently reported adverse events were similar to those reported with other SSRIs and are listed in Table 3. The rates of nausea, insomnia, and headache were similar

to those seen in the paroxetine CR depression trials.[13] Rates of treatment-emergent anxiety (5% paroxetine CR vs. 4% placebo) and nervousness (8% paroxetine CR vs. 7% placebo) were low. No unexpected adverse events occurred, and serious adverse events were uncommon (10 [2.3%] of the 444 patients treated with paroxetine CR, and 8 [1.8%] of the 445 patients treated with placebo). There was no apparent trend in the frequency of abnormal laboratory values or vital signs with paroxetine CR compared with placebo.

At week 10 OC, there was no evidence of a clinically significant change from baseline in body weight in either treatment group (< 1.0-lb mean change). Furthermore, the percentage of patients with significant increases or decreases in weight (defined as ≥ 7% change from baseline) was similar between paroxetine CR– and placebo-treated groups (i.e., 2.7% and 1.6% with significant increases and 2.7% and 1.4% with significant decreases, respectively).

DISCUSSION

The results of this pooled analysis of 3 placebo-controlled studies indicate that paroxetine CR administered for up to 10 weeks is an effective and well-tolerated treatment for panic disorder. During their last 2 weeks of treatment, a significantly greater proportion of patients receiving paroxetine CR were free of full panic attacks compared with placebo-treated patients. The proportion of patients with a CGI-I score of much or very much improved also was greater in patients receiving paroxetine CR versus those receiving placebo. Paroxetine CR was statistically superior to placebo in reducing general anxiety symptoms (based on the HAM-A) and total fear and avoidance (based on the MSPS).

Paroxetine CR was generally well tolerated, with most adverse events being mild to moderate in severity; relatively few patients discontinued paroxetine CR because of adverse events. The adverse event profile was consistent with rates seen in paroxetine CR depression trials[13] and with other SSRIs.[18,19] The difference between rates of treatment-emergent nausea after the first 2 weeks (17% paroxetine vs. 8% placebo) was comparable to that seen in paroxetine CR depression trials after 1 week of treatment (14% paroxetine CR vs. 4% placebo).[13] These rates reflect the higher doses of paroxetine CR (37.5–60 mg) used in the treatment of panic disorder and depression. In this population of patients who are prone to medication intolerance, it is notable that rates of treatment-emergent adverse events were relatively low. Nervousness, anxiety, and agitation were not reported as reasons for study withdrawal with paroxetine CR. This favorable adverse event profile is clinically relevant and may result in enhanced medication adherence, particularly during the initial stages of treatment when the risks of medication nonadherence are high.[20,21]

No evidence of clinically significant weight change was apparent. At endpoint, paroxetine CR–treated patients demonstrated a mean weight loss of less than 1 lb. These findings in a panic disorder population are consistent with the findings of a 32-week paroxetine study in generalized anxiety disorder in which weight gain among paroxetine-treated patients was minimal and similar to that in placebo-treated patients.[22]

Certain limitations to the current analysis should be considered. This article reports the pooled analysis results of all 3 identically designed studies. Paroxetine CR was statistically superior to placebo in the LOCF analysis of the primary efficacy variable in 1 of the 3 studies and in the OC analysis in 2 of the 3 studies. The reliability of panic frequency as an efficacy criterion has been discussed. Our analyses included secondary study parameters such as CGI-I, CGI-S, HAM-A, and MSPS to provide a more complete picture of efficacy. Results of these secondary efficacy measures showed significance in all 3 of the pooled trials of paroxetine CR.

The inclusion of patients with secondary Axis I disorders is another potential study limitation. Nevertheless, the results demonstrate improvement of panic symptoms in the exacerbating context of a comorbid mood or anxiety disorder. This is clinically meaningful to the actual panic disorder patient population, in which depression and other anxiety disorders (e.g., social anxiety disorder) are commonly present.[23]

Finally, our study did not include a paroxetine immediate-release arm, which precludes comparisons of paroxetine IR and paroxetine CR. Side effect profiles for paroxetine CR and the IR formulation were comparable in depression trials that studied doses similar to those used for panic disorder.[13,14] Rates of adverse events 1 to 2 weeks after treatment onset were lower with paroxetine CR compared with paroxetine IR[13,14] and demonstrate an improved tolerability that may lower dropout rates and improve adherence. Follow-up studies would be useful to directly compare the tolerability of paroxetine IR and paroxetine CR in panic disorder treatment.

CONCLUSION

The efficacy and favorable adverse event profile observed in this study make paroxetine CR a rational choice of treatment for panic disorder. Treatment with paroxetine CR results in a reduction in panic disorder frequency and an improvement in symptoms.

Drug name: paroxetine (Paxil and others).

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