Gepirone Extended-Release Treatment of Anxious Depression: Evidence From a Retrospective Subgroup Analysis in Patients With Major Depressive Disorder

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Objective: To evaluate the efficacy and tolerability of gepirone extended-release (ER) tablets in patients with major depressive disorder (MDD) and high ratings of anxiety (anxious depression).

Method: This subgroup analysis was derived from an 8-week, double-blind, placebo-controlled study of gepirone ER in patients with MDD. Male and female patients 18 to 69 years of age who met DSM-IV criteria for MDD and had high ratings of anxiety (Hamilton Rating Scale for Depression [HAM-D-17] total score ≥ 20 and HAM-D-17 factor I [anxiety/somatization] score > 6) were included in this subgroup analysis. Eligible patients with anxious depression were randomly assigned to receive either placebo or gepirone ER, 20 mg to 80 mg daily. Patient assessments were performed at weeks 1, 2, 3, 4, 6, and 8. Treatment efficacy was evaluated by mean HAM-D-17 total scores and mean changes from baseline in (1) HAM-D-17 total scores, (2) HAM-D-17 factor I (anxiety/somatization) scores, and (3) HAM-D-17 item 12 (anxiety, psychic) scores. All statistical tests were 2-sided and considered statistically significant if the p value was < .05. Between-group comparisons were analyzed using least-squares analysis of variance on the change from baseline at each visit with the last observation carried forward (LOCF). The Cochran-Mantel-Haenszel test adjusting for center was also performed on the percentage of patients in each treatment group at each visit (LOCF) who met the response criterion on the HAM-D-17 (≥ 50% decrease from baseline) or remission criterion (HAM-D-17 total score ≤ 7).

Results: Gepirone ER-treated patients (N = 58) experienced a statistically significant (p < .05) reduction in mean HAM-D-17 total score at week 3, 6, and 8 compared with placebo-treated patients (N = 75). A statistically significant effect (p < .05) in favor of gepirone ER was observed in mean change from baseline in HAM-D-17 total scores and for HAM-D factor I (anxiety/somatization) scores from week 2 onward. A statistically significant (p ≤ .01) effect in favor of gepirone ER was observed in HAM-D-17 item 12 (anxiety, psychic) scores throughout the 8-week trial. There were significantly more patients in the gepirone ER group compared with the placebo group who were HAM-D-17 responders (p < .05) at endpoint and who met the criteria for HAM-D-17 remission at week 3 (p < .05) and weeks 6 and 8 (p < .01). Overall, gepirone ER was well tolerated, with rates of weight gain and sexual dysfunction comparable to placebo. Adverse events were generally mild to moderate. The most commonly reported adverse events were dizziness and nausea.

Conclusions: Gepirone ER is an effective and well-tolerated treatment for patients with anxious depression.

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Major depressive disorder (MDD) often occurs with comorbid symptoms of anxiety, and while symptoms of anxiety are not part of the criteria by which major depression is diagnosed, it has been recognized for many years that anxiety may play a critical role in depressive illness.[1–5] Among 2 large outpatient samples with MDD,[6,7] anxiety disorders represented the predominant form of Axis I comorbidity, present in over 40% of depressed patients. General population data available from the U.S. National Comorbidity Survey[8] also indicate that anxiety disorders are the most common primary disorders (58%) associated with MDD. While anxious depression may be defined syndromally as MDD plus a lifetime of current anxiety disorder, a majority of studies

have adopted a dimensional definition, specifically MDD accompanied by moderate to marked anxiety symptoms. The presence of anxiety has been associated with greater severity of depression and functional impairment[9] as well as increased suicide risk.[5,8,10,11] Moreover, anxiety symptoms have been associated with delayed or reduced antidepressant response in some,[4,12–14] but not all,[6,11,15] studies of depressed patients, as well as with greater risk of relapse[14,16] and chronicity.[17] Treatment of anxious depression presents unique challenges, optimally involving pharmacologic agents that are effective for both depression and anxiety.[6,18]

Although the precise etiology of anxious depression is still unclear, numerous studies have suggested that a link exists between anxiety and depression and the action and concentration of serotonin (5-HT) receptors belonging to the 1A subtype.[19–21] Drugs that stimulate 5-HT_{1A} receptors have been found to exhibit antidepressant and anxiolytic properties, and are effective in the treatment of psychiatric patients who have MDD with anxiety.[19,22]

Gepirone extended-release (ER) is a 5-HT_{1A} agonist that has been shown in clinical studies to be effective and well tolerated in patients with MDD.[23–25] Gepirone exhibits substantial first-pass metabolism with the formation of 2 major metabolites, 1-(2-pyrimidinyl)-piperazine (1-PP) and 3'-hydroxy (OH)-gepirone. In preclinical models, 3'-OH-gepirone exhibits full 5-HT_{1A} agonism in the hippocampal CA_3 pyramidal neuron.[26] Similarly, the parent compound, gepirone, binds both presynaptically and postsynaptically to the 5-HT_{1A} receptor and acts as a full agonist in the dorsal raphe.[27] 1-PP is a presynaptic α_2-adrenoceptor antagonist that in animal models of depression does not elicit significant effects.[28] The presence of 3'-OH-gepirone may have some clinical relevance as suggested by recent research suggesting that the magnitude of the psychotropic activity of 5-HT_{1A} receptor ligands is associated with their intrinsic activity at the receptor.[29]

The value of an extended-release formulation is in reducing peak-to-trough plasma fluctuations. Thereby, clinical efficacy can be maintained while minimizing adverse events. Moreover, it is the hope that with fewer daily doses, patient compliance can be enhanced.[30]

Gepirone ER was recently evaluated in a large (N = 208) double-blind trial of outpatients diagnosed with MDD.[23] Findings indicated that patients treated with gepirone ER, 40 mg to 80 mg daily, experienced statistically significant reductions in 17-item Hamilton Rating Scale for Depression (HAM-D-17) total scores. In addition, a significantly greater proportion of patients treated with gepirone ER achieved HAM-D criteria for response and remission versus placebo-treated patients. To evaluate the efficacy and tolerability of gepirone ER in patients with anxious depression, we analyzed a subgroup of depressed patients with anxiety symptoms from the Feiger et al.[23] trial.

METHOD

This subgroup analysis was performed on patients who were part of a larger randomized, double-blind, placebo-controlled, 8-week, multicenter investigation of gepirone ER in patients with MDD as defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV). This study was conducted in full agreement with the Declaration of Helsinki and the principles of Good Clinical Practice at 5 sites in the United States. Written informed consent, which was approved by the institutional review board at each site, was obtained from all patients prior to participation in the study. The design of this multicenter trial has been described in detail elsewhere.[23]

Patient Selection

Patients aged 18 to 69 years who had clinically significant daily dysphoria for the past 4 weeks as determined by the study investigator and met DSM-IV criteria for MDD (screening and baseline HAM-D-17 total score of ≥ 20) were eligible for participation in the study. Patients were excluded from study participation if they had a ≥ 20% decrease in their HAM-D-17 total score between the screening and baseline visits. Additionally, patients with a primary DSM-IV Axis I disorder other than major depressive disorder or with an Axis II disorder were excluded, as were patients with a history of seizure disorder, bipolar disorder, refractory depression, psychoactive substance disorder, or alcohol dependence. Patients with any clinically meaningful medical disorder or clinical laboratory abnormality or those patients currently in psychotherapy or at significant suicidal risk were not eligible for study participation. Any history of electroconvulsive therapy within the past year or treatment with monoamine oxidase inhibitors within 3 weeks, fluoxetine within 5 weeks, or other psychotropic medications within 2 weeks of study start were not eligible for study participation. Women who were pregnant or lactating at screening were excluded.

In contrast to the larger primary study,[23] which included depressed patients with and without anxiety symptoms at baseline, this subgroup analysis included only patients with anxious depression. Anxious depression was defined as a diagnosis of MDD with a baseline HAM-D-17 total score of ≥ 20 and a baseline HAM-D-17 factor I (anxiety/somatization) score of > 6[6,31] (Table 1).

Study Treatments

Study medication was supplied as gepirone ER 20-mg tablets with matching placebo. The initial dose of gepirone ER was 20 mg once daily. On day 4, the dose was increased to 2 gepirone ER 20-mg tablets once daily (40 mg). Based on tolerability and therapeutic response, patients could receive 3 gepirone ER 20-mg tablets once daily (60 mg) after day 7 and 4 gepirone ER 20-mg tablets

Table 1. HAM-D Factor I (anxiety/somatization) Items[a]

HAM-D-17 Item No.	Description
4	Somatic symptoms, gastrointestinal
9	Somatic symptoms, general
12	Anxiety, psychic
13	Anxiety, somatic
14	Hypochondriasis
15	Insight

[a]Based on the Structured Interview Guide for the HAM-D.[32]
Abbreviation: HAM-D-17 = 17-item Hamilton Rating Scale for Depression.

once daily (80 mg) after day 14. If the drug was poorly tolerated, a gepirone ER dose reduction was permitted, but the minimum daily dose was 40 mg. All patients were instructed to take study medication each day with breakfast. No concomitant psychotropic medications (including benzodiazepines and sedative/hypnotics) were allowed during the study period.

Study Assessments

Patient assessments were performed at weeks 1, 2, 3, 4, 6, and 8. The primary efficacy variables in this subgroup analysis included the absolute mean HAM-D-17 total score and the mean change from baseline in HAM-D-17 total scores, HAM-D-17 factor I (anxiety/somatization) scores, and HAM-D-17 item 12 (anxiety, psychic) scores. On the basis of the Structured Interview Guide for the HAM-D (SIGH-D),[32] factor I of the HAM-D includes item 4 (somatic symptoms, gastrointestinal), item 9 (somatic symptoms, general), item 12 (anxiety, psychic), item 13 (anxiety, somatic), item 14 (hypochondriasis), and item 15 (insight) (see Table 1). The HAM-D-17 item 12 was used to inquire about symptoms such as subjective tension and irritability and general worry about minor things. The mean HAM-D-17 total score and the change from baseline for the HAM-D-17 total score, HAM-D-17 factor I score, and HAM-D-17 item 12 score were assessed at each study visit.

Safety and tolerability were assessed by physical examinations, standard laboratory tests, vital signs, electrocardiogram, and spontaneously reported adverse events.

Data Analysis

Efficacy data were analyzed using the intent-to-treat (ITT) population, which included all randomly assigned patients who received at least 1 dose of study medication and who had at least 1 postbaseline efficacy assessment performed. All statistical tests were 2-sided and considered statistically significant if the p value was $< .05$. Tolerability data were analyzed using the all-subjects-treated (AST) population.

Data were analyzed using the last-observation-carried-forward (LOCF) method. Change from baseline to each treatment visit was evaluated by least squares analysis of variance using treatment as the only effect. Additional analyses were performed on the proportion of patients who were responders and those who achieved remission in each treatment group. Responders were defined as patients who had a $\geq 50\%$ decrease from baseline on the HAM-D-17. Remission was achieved if patients had a HAM-D-17 total score of ≤ 7 during treatment. Differences between treatment groups were analyzed using the Cochran-Mantel-Haenszel test adjusting for center on percentage of patients at each visit (LOCF) who met the response criteria.

Table 2. Baseline Demographic and Clinical Profile Information of Patients With Anxious Depression

Characteristic	Gepirone ER	Placebo
Intent-to-treat population, N	58	75
Age		
Mean ± SD	37.0 ± 10.4	41.1 ± 12.5
Range	18–62	19–69
Sex, female/male, %	66/34	55/45
Duration of current episode, N (%)		
1 to 6 months	16 (27.6)	20 (26.7)
7 to 12 months	12 (20.7)	16 (21.3)
> 12 months	30 (51.7)	39 (52.0)
Baseline HAM-D-17 score, mean ± SD		
Total	23.4 ± 2.6	23.3 ± 2.6
Factor I	8.0 ± 1.1	7.8 ± 0.9
Item 12	2.4 ± 0.5	2.1 ± 0.5
All-subjects-treated population, N	61	78
Completed, N (%)	48 (78.7)	61 (78.2)
Discontinued, N (%)	13 (21.3)	17 (21.8)
Adverse event	4 (6.6)	1 (1.3)
Lack of efficacy	3 (4.9)	3 (3.8)
Withdrew consent	2 (3.3)	7 (9.0)
Lost to follow-up	4 (6.6)	6 (7.7)

Abbreviations: ER = extended-release, HAM-D-17 = Hamilton Rating Scale for Depression.

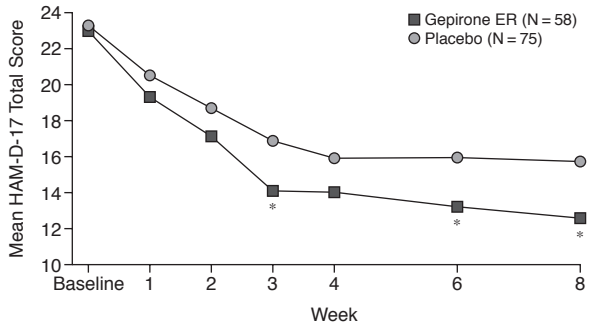
RESULTS

The ITT analysis included 133 male and female patients. Fifty-eight patients received gepirone ER, and 75 patients received placebo. The AST analysis included 139 patients. Sixty-one patients received gepirone ER and 78 received placebo. Baseline demographics for the ITT and AST populations were comparable between the 2 treatment groups. Four patients (6.6%) receiving gepirone ER and 1 patient (1.3%) receiving placebo discontinued treatment due to adverse events, while 3 patients in each group (4.9% gepirone vs. 3.8% placebo) discontinued treatment due to lack of efficacy (Table 2).

Efficacy

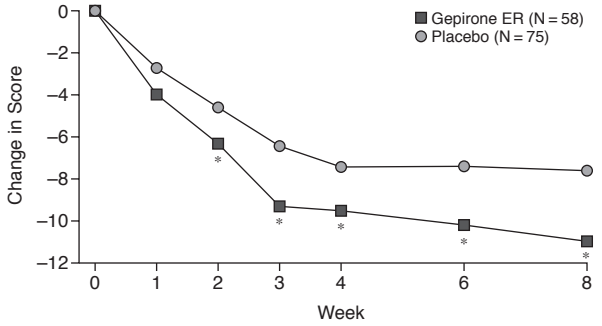
Figure 1 depicts the mean HAM-D-17 total scores at each visit. Both groups showed improvements in mean HAM-D-17 scores with statistical significance in favor of gepirone ER at weeks 3, 6, and 8. For the mean change from baseline in the HAM-D-17 total score, the gepirone ER group had statistically significantly greater decreases versus placebo as early as week 2 through the

Figure 1. Gepirone ER Versus Placebo for Anxious Depression



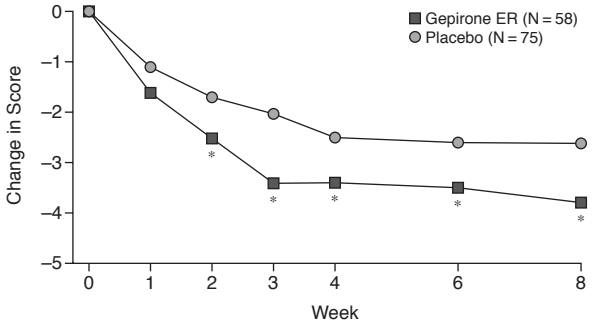
*p < .05.
Abbreviations: ER = extended-release, HAM-D-17 = 17-item Hamilton Rating Scale for Depression.

Figure 2. Mean Change From Baseline in HAM-D-17 Total Scores for Patients With Anxious Depression[a]



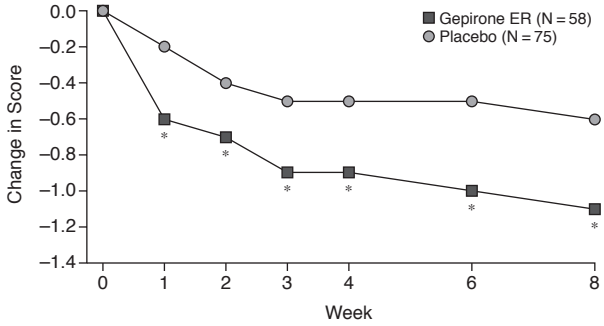
[a]Negative values signify reductions in total scores.
*p < .05.
Abbreviations: ER = extended-release, HAM-D-17 = Hamilton Rating Scale for Depression.

Figure 3. Mean Change From Baseline in HAM-D-17 Factor I (anxiety/somatization) Score[a]



[a]Negative values signify reductions in factor I scores.
*p < .05.
Abbreviations: ER = extended-release, HAM-D-17 = 17-item Hamilton Rating Scale for Depression.

Figure 4. Mean Change From Baseline in HAM-D-17 Item 12 (anxiety, psychic) Score[a]



[a]Negative values signify reductions in item 12 scores.
*p ≤ .01.
Abbreviations: ER = extended-release, HAM-D-17 = 17-item Hamilton Rating Scale for Depression.

end of the trial. The overall mean ± SD change from baseline was –10.9 ± 7.6 and –7.6 ± 6.8 for gepirone ER and placebo, respectively ($p < .05$) (Figure 2). Absolute mean baseline HAM-D-17 total scores were 23.4 ± 2.6 for gepirone ER and 23.3 ± 2.6 for placebo. At endpoint, the mean gepirone ER HAM-D-17 total score was 12.5 ± 8.3 compared with the placebo score of 15.7 ± 7.2.

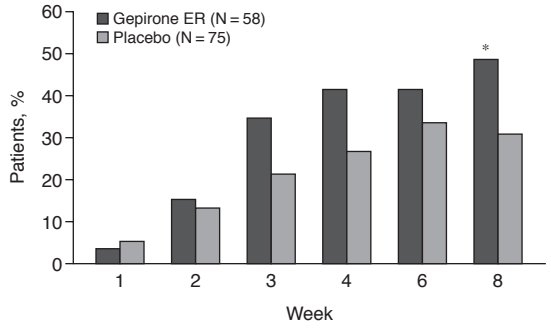
The observed therapeutic effect of gepirone ER on HAM-D-17 factor I (anxiety/somatization) scores is depicted in Figure 3. The figure shows mean changes from baseline in the severity of anxious/somatic symptoms for gepirone ER versus placebo treatment during the 8-week trial. Patients receiving gepirone ER reported significantly greater improvement versus placebo at all time points beginning at week 2 until the end of the trial ($p < .05$). At endpoint, the change from baseline in factor I scores for the gepirone ER group was –3.8 ± 3.0 compared with the change in the placebo group of only –2.6 ± 2.5.

The mean changes from baseline in HAM-D-17 item 12 scores for gepirone ER versus placebo treatment during the 8-week trial is depicted in Figure 4. Patients receiving gepirone ER reported statistically significantly greater improvement versus placebo at all time points ($p \leq .01$). At endpoint, the item 12 mean change from baseline score was –1.1 ± 1.0 compared with –0.6 ± 0.8 for gepirone ER- and placebo-treated patients, respectively.

Response and Remission

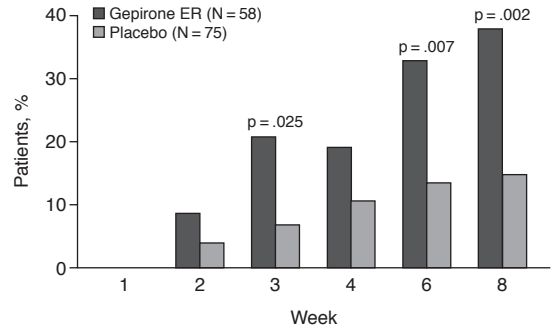
The proportion of patients in each treatment group who were HAM-D-17 responders (defined as a ≥ 50% decrease from baseline in HAM-D-17 total score) is represented in Figure 5. There were more responders in the gepirone ER group compared with placebo beginning at week 2. This was statistically significantly different in favor of gepirone ER at the week 8 visit (48.3% [28/58]

Figure 5. Response Rate in Patients With Anxious Depression Taking Gepirone ER or Placebo[a]



[a]Response defined as a ≥ 50% decrease from baseline in HAM-D-17 total score.
*p = .035.
Abbreviations: ER = extended-release, HAM-D-17 = 17-item Hamilton Rating Scale for Depression.

Figure 6. HAM-D-17 Remission Rate in Patients With Anxious Depression Taking Gepirone ER or Placebo[a]



[a]Remission of depressive symptoms defined as a HAM-D-17 total score of ≤ 7.
Abbreviations: ER = extended-release, HAM-D-17 = 17-item Hamilton Rating Scale for Depression.

vs. 30.7% [23/75], p = .035). The proportion of patients achieving remission (defined as a HAM-D-17 total score of ≤ 7) is shown in Figure 6. There were significantly more patients in the gepirone ER group who achieved remission overall compared with patients in the placebo group and this was significantly different in favor of gepirone ER at weeks 3, 6, and 8. At endpoint, there were 37.9% (22/58) gepirone ER patients compared with 14.7% (11/75) placebo patients who were in remission (p = .002).

High Versus Low Levels of Anxiety

A separate analysis in gepirone ER-treated patients was conducted comparing patients with anxious depression at baseline to the group of patients from the original study with low anxiety at baseline (without anxious depression). This was in contrast to the subgroup analysis above, which compared gepirone ER to placebo in patients with anxious depression. The purpose of this separate analysis was to determine whether anxiety level is a predictor of response. The 58 gepirone ER-treated patients with high levels of anxiety (HAM-D-17 factor I score of > 6 at baseline) were compared with the 43 gepirone ER patients from the larger primary study without anxious depression (HAM-D-17 factor I score of ≤ 6 at baseline). As might be expected, there were significant differences between these 2 groups in the mean baseline HAM-D-17 total score, HAM-D-17 factor I score, and HAM-D-17 item 12 score. Although there were slightly more patients who met the criteria for a response in the high anxiety group, there was no significant difference in the proportion of responders at endpoint (48.3% [28/58] high anxiety vs. 37.2% [16/43] low anxiety, p = .41), or in the mean change in HAM-D-17 total score or HAM-D-17 item 12 score. There were, however, significantly more patients who met the criteria for remission in the high anxiety group (37.9% [22/58]) compared with the low anxiety group (16.3% [7/43], p = .02), and the high anxiety group had a greater decrease from baseline in mean HAM-D-17 factor I score compared with the low anxiety group (p < .001).

Table 3. Incidence (%) of Adverse Events Occurring in at Least 10% of Patients by Treatment Received (all-subjects-treated population)

Adverse Event	Gepirone ER (N = 61)	Placebo (N = 78)
Diarrhea	16.4	14.1
Dizziness	55.7*	12.8
Headache	34.4	25.6
Insomnia	14.8	9.0
Nausea	36.1*	14.1
Nervousness	13.1	6.4
Somnolence	8.2	12.8

*p < .05.

Tolerability

All adverse events were coded using a modified version of COSTART-5. The incidence of adverse events occurring in at least 10% of patients in the gepirone ER group or the placebo group is listed in Table 3. More patients in the gepirone ER group reported dizziness and nausea compared with the placebo group. Only 2 gepirone ER–treated patients (3.3%) discontinued therapy due to dizziness.

No clinically significant changes in laboratory parameters, physical examinations, vital signs, or ECG parameters were observed in either treatment group. Somnolence was not prevalent in gepirone ER–treated patients (8.2% [5/61] of the gepirone ER–treated group versus 12.8% [10/78] of the placebo group reported somnolence). Weight gain was not prevalent in gepirone ER–

treated patients (3.3% [2/61] of the gepirone ER–treated group and 2.6% [2/78] of the placebo group reported weight gain). This difference was not statistically significant. Based on spontaneous adverse event reporting, fewer gepirone ER–treated patients reported abnormal sexual function (0.0% [0/61] vs. 2.6% [2/78]) and libido decrease (1.6% [1/61] vs. 2.6% [2/78]) than those patients treated with placebo.

DISCUSSION

This subgroup analysis demonstrates that gepirone ER, a 5-HT_{1A} agonist, is an effective and well-tolerated treatment for patients with anxious depression when administered at doses ranging from 40 mg to 80 mg daily. In this analysis, patients receiving gepirone ER experienced significantly greater improvements than those taking placebo within 1 to 2 weeks after the start of treatment. Specifically, patients treated with gepirone ER experienced significant improvements in all efficacy measures, including the absolute mean HAM-D-17 total score, mean change from baseline in scores for HAM-D-17 total, HAM-D factor I (anxiety/somatization) scores, and HAM-D item 12 (anxiety, psychic) scores, as well as response and remission rates.

These findings are similar to those reported by Feiger and colleagues[23] for the overall study population. In the present analysis, there was a statistically significant improvement in favor of gepirone ER on the HAM-D-17 total score compared with placebo at weeks 3, 6, and 8. Both the mean change in HAM-D-17 total score and the mean change in factor I (anxiety/somatization) score was statistically significant compared with placebo beginning at week 2, and this improvement continued throughout the trial. HAM-D item 12 (anxiety, psychic) scores were significantly improved compared with placebo at all post-baseline visits, illustrating the potentially early anxiolytic effects of gepirone ER. At treatment end, HAM-D-17 response rates in this analysis were similar to those reported in the larger study, while HAM-D-17 remission rates at treatment end were higher in this analysis for gepirone ER patients (37.9% vs. 28.7% in the overall study).

The presence of anxiety symptoms did not appear to delay or reduce the antidepressant response to gepirone ER. Whether, on the other hand, level of anxiety is a positive predictor of response to gepirone ER is not conclusive. There were better responses to gepirone ER for all variables measured among individuals with anxious versus nonanxious MDD; however, only when measuring the proportion of patients showing remission and measuring mean changes in HAM-D-17 factor I scores were the results statistically significant.

Gepirone ER was well tolerated among patients with anxious depression, with dizziness being the most common side effect, typical of 5-HT_{1A} agonists.[33,34] Patients and investigators used several different terms to describe what was typically a mild, transitory, vague sense of lightheadedness, all of which fall under the COSTART-5 category "dizziness." Of the 55.7% of gepirone ER–treated patients in this subgroup analysis who reported some lightheadedness or dizziness, only 3.3% (2 patients) discontinued treatment due to this adverse event. The incidence of adverse events in the subgroup analysis was similar to that in the primary study by Feiger et al.[23]

The phenomenon of somatic symptoms such as dizziness within antidepressant trials raises interesting etiological questions. In an evaluation of over 200 patients with dizziness, Eckhardt-Henn et al.[35] reported that 72% of these patients' dizziness was the result of either psychogenic or comorbid psychiatric conditions. There are also reports in the literature indicating that for many patients with dizziness, psychiatric disorders appear to exert an important influence on this condition.[36,37] Dizziness is the most commonly reported symptom of selective serotonin reuptake inhibitor discontinuation syndrome.[38] Further investigations of this phenomenon within trials are warranted.

No falls were reported by patients in either the gepirone ER or placebo groups. Sedation is not a characteristic side effect of gepirone; in fact, more placebo patients (12.8%) reported feelings of somnolence compared with gepirone ER patients (8.2%). Weight gain and sexual dysfunction were not associated with gepirone ER treatment in this 8-week study.

Despite the positive findings of this analysis, several limitations exist. First, the lack of an active comparator hinders interpretation of these findings. To fully understand the effect of gepirone ER in the treatment of anxious depression, a comparison trial is needed with an antidepressant with established efficacy for treating symptoms of anxiety. Second, the use of a factor score and an individual psychic anxiety item on the HAM-D provides a more limited appraisal of anxiety than specific anxiety rating scales, such as the Hamilton Rating Scale for Anxiety.[39] Finally, although depression with anxiety symptoms is thought to overlap with depression with 1 or more anxiety disorders, the extent of overlap was not studied in this sample and we restrict our conclusions to patients with depression.

In summary, the findings of this analysis provide evidence for the antidepressant and anxiolytic effects of the 5-HT_{1A} agonist gepirone ER. Gepirone ER treatment resulted in early and consistently greater reductions in depression and symptoms of anxiety compared with placebo treatment. Additionally, this analysis provides evidence that psychic and somatic anxiety, 2 of the core anxiety symptoms found in depression, are reduced with gepirone ER treatment. The majority of anxiously depressed patients in this analysis tolerated doses of 40 mg to 80 mg daily, with no clinically relevant safety issues reported,

and sexual dysfunction, weight gain, and sedation did not emerge as common side effects. The overall results of this analysis indicate that gepirone ER appears effective and well-tolerated in the short-term treatment of anxious depression.

Drug name: fluoxetine (Prozac and others).

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