Assessing the Efficacy of Desvenlafaxine for Improving Functioning and Well-Being Outcome Measures in Patients With Major Depressive Disorder: A Pooled Analysis of 9 Double-Blind, Placebo-Controlled, 8-Week Clinical Trials

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Objective: To evaluate the effects of desvenlafaxine therapy on functioning and well-being in major depressive disorder (MDD).

Method: Total and individual item Sheehan Disability Scale (SDS) and 5-item World Health Organization Well-Being Index (WHO-5) scores from 8 double-blind, placebo-controlled, 8-week desvenlafaxine clinical trials were pooled. Scores on the 17-item Hamilton Depression Rating Scale (HDRS₁₇) work/activities and Montgomery-Asberg Depression Rating Scale (MADRS) lassitude items were pooled from 9 studies. Outpatients with DSM-IV MDD were randomly assigned to fixed (5 studies; 50, 100, 200, or 400 mg/d; n = 1,342) or flexible (4 studies, 100-400 mg/d; n = 463) doses of desvenlafaxine or placebo (n = 1,108). Data from each patient's final evaluation were analyzed for the total population and for individual dose groups from the fixed-dose studies and were compared between groups using analysis of covariance.

Results: Compared with placebo, desvenlafaxine therapy resulted in significantly greater improvements in SDS total score (-2.0) and individual items regarding work (-0.6), social life/ leisure activities (-0.8), and family life/home responsibilities (-0.7; P<.001 for all comparisons), as well as WHO-5 total score (1.7) and individual items (good spirits [0.4], calm/relaxed [0.4], active/vigorous [0.3], fresh/rested [0.3], and interest [0.3]; *P*<.001 for all comparisons). Desvenlafaxine treatment resulted in significant improvements on the HDRS₁₇ work/activities (-0.2; *P* < .001) and MADRS lassitude (-0.3; P < .001) items compared with placebo. Significant differences were observed for the individual fixeddose groups on all outcomes (P < .05); there was no evidence of a dose-response relationship.

Conclusions: Desvenlafaxine therapy resulted in significant improvements in the functioning and well-being among MDD patients.

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A number of large-scale longitudinal studies have demonstrated that patients with major depressive disorder (MDD) experience significant impairment in daily functioning, including work performance¹⁻⁴ and psychosocial functioning.⁵⁻⁷ The National Comorbidity Survey Replication found that individuals with MDD are unable to work or perform their usual daily activities for an average of 35 days per year.⁸ In terms of work functioning, depressed employees annually lose approximately 9 days to absenteeism and 18 days to *presenteeism*, the latter defined as days that employees are present at work yet do not optimally perform their daily activities.⁹ Impairments in family and social functioning, as well as in overall quality of life, have been similarly observed.^{10,11}

Despite accumulated data demonstrating that a diagnosis of MDD is associated with impairment in real-world functioning, clinical trials that assess the efficacy of antidepressant pharmacotherapy traditionally focus on only the emotional and physical components of depression. More recently, outcome measures that evaluate the impact of MDD on daily functioning have become more routinely used as end points in antidepressant clinical trials.¹² Results from the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) trial demonstrated not only that antidepressant therapy improves psychosocial functioning, work functioning, and quality of life, but also that these factors are significantly related to improvement in overall depressive symptomatology.¹³

The aim of the current analysis was to assess the efficacy of desvenlafaxine (administered as desvenlafaxine succinate) for reducing impairment in functioning and well-being associated with MDD. Desvenlafaxine, a serotonin-norepinephrine reuptake inhibitor, is the major active metabolite of the antidepressant venlafaxine¹⁴ and has been approved for the treatment of MDD.¹⁵

METHOD

Study Design

Scores on the Sheehan Disability Scale (SDS)¹⁶ and the 5-item World Health Organization Well-Being Index (WHO-5)¹⁷ were pooled from 8 of the 9 desvenlafaxine registration trials, ie, those that employed these outcome measures while assessing study participants. In addition, the 17-Item Hamilton Depression Rating Scale (HDRS₁₇)¹⁸ work and activities and Montgomery-Asberg Depression Rating Scale (MADRS)¹⁹ lassitude items were pooled from all 9 registration studies (Table 1). These studies used a randomized, short-term (8 weeks), placebo-controlled, double-blind design to assess the efficacy, safety, and tolerability of desvenlafaxine for treating MDD. Patients received either fixed (50 mg/d [2 studies]; 100 mg/d [3 studies]; 200 mg/d [3 studies]; 400 mg/d [3 studies]) or flexible doses (100 to 200 mg/d [1 study]; 200 to 400 mg/d [3 studies]) of desvenlafaxine or an identically appearing placebo.

Patients

Outpatients at least 18 years of age meeting *Diagnostic* and Statistical Manual of Mental Disorders, Fourth Edition²⁰ criteria for MDD were enrolled in each study. Screening and baseline HDRS₁₇ total scores \geq 20 or \geq 22, or MADRS score \geq 24 were required for enrollment. Exclusion criteria were designed to select a population of medically stable patients with MDD. A full description of the individual study populations assessed here are described in the primary publications^{21–27} of these studies as well as an integrated analysis of efficacy based on data from these 9 studies (data on file, Wyeth Research, Collegeville, Pennsylvania).

Functional and Psychosocial Outcome Assessments

The SDS and WHO-5 were administered at baseline and at weeks 2, 4, and 8. The SDS individual domains of work, social life/leisure activities, and family life/home responsibilities are self-rated and use an 11-point Likert response scale (0 = no impairment, 10 = extreme impairment) to assess work, social, and family functioning during the past month. The WHO-5 is a self-report questionnaire that measures positive psychological well-being using the following 5 items: good spirits, calm/relaxed, active/vigorous, fresh/rested, and interested in activities. Total scores range from 0 to 25, with higher score being indicative of improved well-being.¹⁷

Patients were also evaluated with the HDRS₁₇, which was administered at baseline and at weeks 1, 2, 3, 4, 6, and 8, and the MADRS, which was administered at baseline and at weeks 2, 4, and 8. Because the HDRS₁₇ work and activities and MADRS lassitude items assess the difficulty patients might have initiating and performing daily activities, they were also reported in this analysis. The HDRS₁₇ work and activities item assesses the patient's functional ability on a scale of 0 (no difficulty) to 4 (stopped working because of

present illness). Like the other MADRS items, lassitude is rated on a scale of 0 (hardly any difficulty getting started; no sluggishness) to 6 (complete lassitude; unable to do anything without help). For both items, higher scores are indicative of greater symptom severity.

Statistical Analysis

The intent-to-treat (ITT) population was used for the analyses in this study. The ITT population included all randomly assigned patients who had a baseline primary efficacy evaluation, took at least 1 dose of double-blind study medication, and had at least 1 on-therapy primary efficacy evaluation. Analyses of the SDS and WHO-5 are based on data from the 8 studies that included these outcome measures, while the analysis of the HDRS₁₇ work and activities and MADRS lassitude items were based on data from all 9 studies. The primary efficacy time point was each patient's final evaluation, using last-observation-carried-forward (LOCF) data; data for each scheduled visit (LOCF) were also analyzed. Scores on these outcome measures were compared between groups using an analysis of covariance model with the baseline score as covariate, adjusted by protocol to test the treatment effect. In addition, data for the individual fixeddose desvenlafaxine groups and the corresponding placebo groups were pooled separately to allow for examination of efficacy at each dose. To facilitate comparisons across studies and various data sets, outcomes are reported as adjusted mean drug versus placebo differences.

A multiple regression analysis was conducted, controlling for differences in protocol, using treatment group (desvenlafaxine or placebo), gender, race/ethnicity (white, black, Hispanic, other), age, baseline severity, and the interaction of treatment effect by age, race, gender, and baseline severity to identify how these factors relate to improvements on the SDS and WHO-5 for the study group.

RESULTS

Patients

The ITT population included 1,805 desvenlafaxinetreated patients and 1,108 placebo-treated patients (Table 1). Demographic and baseline characteristics of the ITT population are presented in Table 2. Mean baseline total scores on the SDS (desvenlafaxine: 19.3; placebo: 19.7), WHO-5 (desvenlafaxine: 5.8; placebo: 5.8), HDRS₁₇ (desvenlafaxine: 23.9; placebo: 24.0), and the MADRS (desvenlafaxine: 30.5; placebo: 30.5) were comparable between treatment groups.

Functional and Psychosocial Outcome Assessments

SDS. For patients treated with desvenlafaxine, SDS total adjusted mean scores improved throughout the 8-week treatment period to a greater degree than for those receiving placebo (Figure 1). At the final assessment, adjusted mean SDS total scores were significantly lower for patients treated with desvenlafaxine in the total pooled population (11.5)

			Group,	Total,
Study No.	Design	Treatment Group	n	n
Flexible dose				
304^{24}	Phase 3	Placebo	114	234
		Desvenlafaxine 100–200 mg/d	120	
309 ²³	Phase 3	se 3 Placebo		236
		Desvenlafaxine 200-400 mg/d	116	
317^{23}	Phase 3	Phase 3 Placebo		235
		Desvenlafaxine 200-400 mg/d	110	
320 ²⁸	Phase 3	Placebo	118	235
		Desvenlafaxine 200-400 mg/d	117	
Fixed dose		-		
223 ^{29,a}	Phase 2	Placebo	78	213
		Desvenlafaxine 200 mg/d	63	
		Desvenlafaxine 400 mg/d	72	
306 ²²	Phase 3	Placebo	118	461
		Desvenlafaxine 100 mg/d	114	
		Desvenlafaxine 200 mg/d	116	
		Desvenlafaxine 400 mg/d	113	
308 ²⁶	Phase 3	Placebo	124	369
		Desvenlafaxine 200 mg/d	121	
		Desvenlafaxine 400 mg/d	124	
332 ²⁵	Phase 3	Placebo	150	447
		Desvenlafaxine 50 mg/d	150	
		Desvenlafaxine 100 mg/d	147	
333 ²¹	Phase 3	Placebo	161	483
		Desvenlafaxine 50 mg/d	164	
		Desvenlafaxine 100 mg/d	158	
Total		Placebo	1,108	2,913
		Desvenlafaxine	1,805	

Table 1. Studies Included in the Pooled Analysis of Subjects With Major Depressive Disorder Randomly Assigned to Treatment With Desvenlafaxine or Placebo; ITT Population

^aThis study did not include the Sheehan Disability Scale and the 5-item World Health Organization Well-Being Index. Analyses of these outcomes include data from studies 304, 306, 308, 309, 317, 320, 332, and 333 only. Abbreviation: ITT = intent to treat.

compared with placebo (13.5; P < .001). Similar results were seen when analyzing the individual fixed doses and the pooled fixed-dose population—desvenlafaxine 50 mg/d: 10.7; 100 mg/d: 11.0; 200 mg/d: 11.7; 400 mg/d: 11.1; total fixed-dose—11.0; placebo: 13.0 to 14.2 (P < .001 for all comparisons). Additionally, as presented in Table 3, the adjusted mean differences from placebo for each individual SDS item suggest significantly greater improvements in disability for patients treated with desvenlafaxine for each of the individual dose subgroups and the pooled desvenlafaxine group (P < .05 for all comparisons); adjusted mean scores on the individual SDS items at the final evaluation are depicted in Figure 2.

WHO-5. Significantly greater improvements in WHO-5 total scores were observed throughout the treatment period for desvenlafaxine-treated patients compared with those receiving placebo (Figure 3). At the final evaluation, adjusted mean scores for the desvenlafaxine group were significantly higher in the total pooled population (12.7) compared with placebo (11.0; P < .001). For patients treated with fixed doses of desvenlafaxine, significant improvements (50 mg/d: 13.4; 100 mg/d: 13.2; 200 mg/d: 12.7; 400 mg/d: 12.7) were also observed in relation to placebo (10.3–11.7; P < .001 for all comparisons). When analyzing the pooled fixed-dose

Table 2. Demographic and Baseline Characteristics; ITT Population

	DI 1	D 1.C '	
	Placebo	Desvenlafaxine	
Characteristic	(n=1,108)	(n = 1,805)	
Age, mean (SD), y	42.4 (12.7)	42.5 (12.6)	
Female gender, n (%)	709 (64)	1,096 (61)	
Ethnic origin, n (%)			
White	907 (82)	1,501 (83)	
Black	105 (9)	153 (8)	
Hispanic	49 (4)	79 (4)	
Other	47 (4)	72 (4)	
Duration of current episode,	17.7 (39.9)	17.3 (34.6)	
mean (SD), mo			
HDRS ₁₇ score, mean (SD)			
Total	24.0 (3.1)	23.9 (3.0)	
Work and activities item	2.8 (0.5)	2.9 (0.5)	
SDS total score, mean (SD) ^a	19.7 (5.4)	19.3 (5.4)	
WHO-5 total score, mean (SD) ^a	5.8 (3.6)	5.8 (3.6)	
MADRS score, mean (SD)			
Total	30.5 (4.5)	30.5 (4.2)	
Lassitude item	3.5 (0.8)	3.6 (0.8)	

^aMean SDS and WHO-5 scores based on data pooled from 8 short-term, double-blind, placebo-controlled studies that assessed patients with these outcome measures.

Abbreviations: $HDRS_{17} = 17$ -item Hamilton Depression Rating Scale, ITT = intent to treat, MADRS = Montgomery-Asberg Depression Rating Scale, SDS = Sheehan Disability Scale, WHO-5 = 5-item World Health Organization Well-Being Index.

population, the WHO-5 score at the final evaluation was 13.1 for desvenlafaxine-treated patients compared with 11.0 for those receiving placebo (P<.001). Significant differences from placebo in adjusted means for the individual WHO-5 items among patients in the individual desvenlafaxine dose groups and the pooled population were also observed (P<.05; Table 3); adjusted mean scores for each WHO-5 individual item at the final evaluation are depicted in Figure 4.

HDRS₁₇ Work and Activities

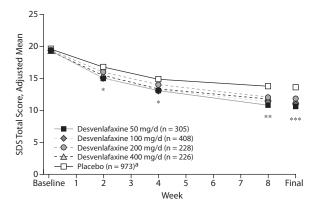
Adjusted mean scores on the HDRS₁₇ work and activities item at the final evaluation for desvenlafaxine 50 mg/d (1.4), 100 mg/d (1.5), 200 mg/d (1.6), 400 mg/d (1.6), the pooled fixed-dose population (1.5), and the total pooled population (1.6) improved to a significantly greater degree compared with placebo (1.7–1.9; $P \le .001$ for all comparisons; Table 3; Figure 5).

MADRS Lassitude

Significantly lower adjusted mean scores on the MADRS lassitude item were observed for desvenlafaxine 50 mg/d (1.7), 100 mg/d (1.9), 200 mg/d (1.9), 400 mg/d (1.8), the pooled fixed-dose population (1.8), and the total pooled population (1.9) compared with placebo (2.0 to 2.3; P < .01 for all comparisons) at the final evaluation (Table 3; Figure 6).

Baseline Predictor Analysis

After controlling for variations in study protocol, treatment group assignment, gender, race/ethnicity, age, and Figure 1. Sheehan Disability Scale (SDS) Total Score Change From Baseline With Desvenlafaxine (LOCF); ITT Population

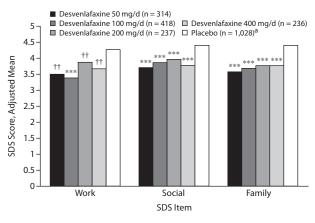


^aPlacebo values are based on the total pooled population. *P* values are based on individual-dose comparisons with their respective placebo groups.

*P<.05 desvenlafaxine 50, 100, and 400 mg/d versus placebo.</p>
**P<.01 desvenlafaxine 50, 100, 200, and 400 mg/d versus placebo.</p>
***P<.001 desvenlafaxine 50, 100, 200, and 400 mg/d versus placebo.</p>

Abbreviations: ITT = intent to treat, LOCF = last observation carried forward.

Figure 2. Adjusted Mean Scores on Sheehan Disability Scale (SDS) Individual Items With Desvenlafaxine at the Final Evaluation; ITT Population



^aPlacebo values are based on the total pooled population. *P* values are based on individual-dose comparisons with their respective placebo

groups.

 $\dagger \dagger P \leq .01.$

****P*<.001 desvenlafaxine versus placebo.

Abbreviation: ITT = intent to treat.

Table 3. Adjusted Mean Difference in Outcome Assessment Scores From Placebo-Treated Patients Among Patients Treated With Desvenlafaxine at the Final Evaluation; ITT Population

Measure					
	50 mg/d (n=314)	100 mg/d (n=418)	200 mg/d (n = 237)	400 mg/d (n = 236)	Total (n = 1,668)
HDRS ₁₇ ^b					
Work/activities	-0.3†††	-0.3†††	-0.3†††	-0.3†††	-0.2^{+++}
MADRS ^b					
Lassitude	-0.3††	-0.3†††	$-0.4^{\dagger}^{\dagger}^{\dagger}^{\dagger}$	-0.5^{+++}	-0.3†††
SDS					
Work	-0.6^{++}	-0.8^{+++}	-0.6^{++}	-0.8^{++}	-0.6†††
Social	-0.9^{+++}	-0.8^{+++}	$-0.9^{\dagger\dagger\dagger}$	-1.2^{+++}	-0.8^{+++}
Family	-0.8^{+++}	$-0.9^{\dagger\dagger\dagger}$	$-0.9^{\dagger\dagger\dagger}$	$-0.9^{\dagger}^{\dagger}^{\dagger}^{\dagger}$	-0.7^{+++}
Total	-2.3†††	-2.3†††	$-2.4^{\dagger}^{\dagger}^{\dagger}$	-3.0†††	-2.0^{+++}
WHO-5					
Good spirits	0.4†††	0.5†††	0.6†††	0.6†††	0.4†††
Calm/relaxed	0.4†††	0.5†††	0.5†††	0.5†††	0.4†††
Active/vigorous	0.3††	0.3†††	0.4^{+++}	0.5†††	0.3†††
Fresh/rested	0.4†††	0.3†††	0.4††	0.3*	0.3†††
Interest	0.3††	0.4†††	0.4†††	0.5†††	0.3†††
Total	1.7†††	2.0†††	2.3†††	2.4†††	1.7†††

^aTotal number of desvenlafaxine-treated patients from all studies that included the SDS and WHO-5 as outcome measures.

^bAnalyses of the HDRS₁₇ and MADRS are based on the 9-study, pooled population (desvenlafaxine 50 mg/d, n = 314; 100 mg/d, n = 419; 200 mg/d, n = 300; 400 mg/d, n = 309; total desvenlafaxine, n = 1,805; placebo, n = 1,108).

*P < .05 desvenlafaxine versus placebo.

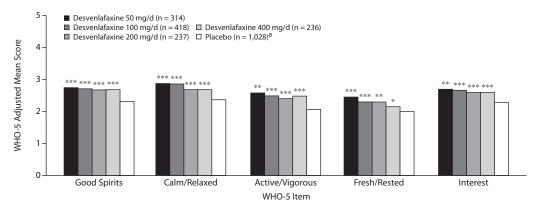
 $\dagger \dagger P \leq .01.$

 $\dagger \dagger \dagger P \leq .001.$

Abbreviations: HDRS₁₇ = 17-item Hamilton Depression Rating Scale, ITT = intent to treat, MADRS = Montgomery-Asberg Depression Rating Scale, SDS = Sheehan Disability Scale, WHO-5 = 5-item World Health Organization Well-Being Index.

baseline severity, younger age was found to predict a larger improvement in functionality, as measured by SDS total score (P < .05), and Hispanic ethnicity could predict greater improvements on the WHO-5 (P < .05) than other groups. The treatment effect is confounded with the baseline severity. On the SDS, the predicted treatment effect of desvenlafaxine over placebo increased as baseline impairment increased; specifically, the treatment effect increased by approximately 0.18 points (P < .01) for each 1-point increase in baseline SDS total score. For the WHO-5, the treatment effect of desvenlafaxine over placebo decreased as baseline well-being increased; specifically, the treatment effect decreased by about 0.24 points (P < .001) as the baseline WHO-5 total score increased by 1 point.

Figure 4. Adjusted Mean Scores on WHO-5 Individual Items With Desvenlafaxine at the Final Evaluation; ITT Population

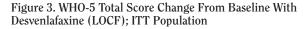


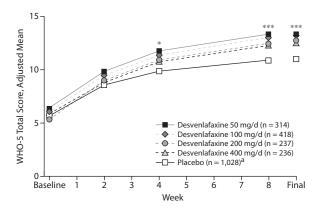
^aPlacebo values are based on the total pooled population. P values are based on individual-dose comparisons with their respective placebo groups.

**P*<.05 desvenlafaxine versus placebo.

P*<.01. *P*<.001.

Abbreviations: ITT = intent to treat, WHO-5 = 5-item World Health Organization Well-Being Index.





^aPlacebo values are based on the total pooled population. *P* values are based on individual-dose comparisons with their respective placebo groups.

*P<.05 desvenlafaxine 50, 100, and 400 mg/d versus placebo.
 ***P<.001 desvenlafaxine 50, 100, 200, and 400 mg/d versus placebo.
 Abbreviations: ITT = intent to treat, LOCF = last observation carried forward, WHO-5 = 5-item World Health Organization Well-Being Index.

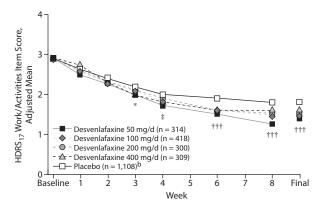
Adverse Events

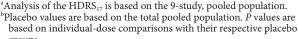
The most common treatment-emergent adverse events (incidence $\geq 10\%$ in any desvenlafaxine group and at least twice the incidence observed for placebo) were asthenia, anorexia, constipation, nausea, dry mouth, dizziness, somnolence, and sweating. Across all doses studied, rates of discontinuation due to adverse events were 12% with desvenlafaxine and 3% with placebo. However, attrition due to adverse events was heavily dependent on the dose of desvenlafaxine, ranging from 4.1% on 50 mg/d to 17.7% on 400 mg/d. Safety and tolerability outcomes for this data set have been presented in their entirety elsewhere.³⁰

DISCUSSION

Desvenlafaxine has previously demonstrated efficacy in alleviating the broad spectrum of physical and emotional depressive symptoms that are associated with MDD.^{22,24,27} In the current pooled analysis of individual patient data from the entire set of placebo-controlled studies of desvenlafaxine for treating MDD, efficacy was established for functional outcomes relevant to patients, including a range of work, social, and family activities. When exploring these outcomes in the individual studies, all but 1 fixed-dose desvenlafaxine treatment arm (100 mg/d)²⁵ demonstrated significant improvement in relation to their respective placebo groups on SDS and WHO-5 total score (50 mg/d,^{21,25} 100 mg/d,^{21,22} 200 mg/d, 22,26 400 mg/d 22,26). Less consistent efficacy on these outcome measures was observed when flexible doses of desvenlafaxine were used (100 to 200 mg/d,²⁴ 200 to 400 mg/d^{23,28}). In 1 of the 2 studies that included a venlafaxine extended release 75 to 150 mg comparator arm, patients experienced significant improvements on the SDS and WHO-5 compared with placebo.²³

Disability assessments and functional outcome measures have only recently become recognized as important outcome measures in antidepressant clinical trials, and the variety of available scales that assess such outcomes makes comparisons between clinical trials somewhat difficult. However, the SDS is believed to be one of the most effective measures of disability for use in antidepressant clinical trials because of its sensitivity in detecting treatment effects and its ease of use.³¹ In a pooled analysis of 2 placebo-controlled clinical trials that compared the efficacy Figure 5. HDRS₁₇ Work and Activities Item Change From Baseline Scores With Desvenlafaxine (LOCF); ITT Population^a



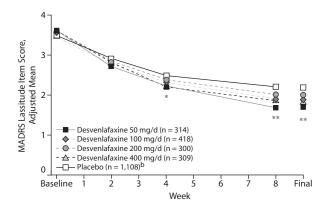


groups. *P<.05 desvenlafaxine 50, 100, and 400 mg/d versus placebo. ‡P<.05 desvenlaxine 50, 100, 200, and 400 mg/d versus placebo. †††P<.001 desvenlafaxine 50, 100, 200, and 400 mg/d versus placebo. Abbreviations: ITT = intent to treat, LOCF = last observation carried forward, HDRS₁₇=17-item Hamilton Depression Rating Scale.

of duloxetine (80 and 120 mg/d), paroxetine (20 mg/d), and placebo for the treatment of MDD, patients receiving both active treatments had a total mean baseline SDS score of 19.7, which was comparable to the 19.3 baseline score presented here, and a change from baseline to week 8 of -8.9, which is also comparable to the -8.0 change from baseline presented here.³²

Although mean scores on the SDS (10.7 to 11.7) for the desvenlafaxine-treated group did not reach levels indicative of normative functioning (ie, $< 5^{33}$) after 8 weeks of treatment, the final scores on the WHO-5 for the desvenlafaxine groups improved to levels (12.7 to 13.4) that were generally above the threshold commensurate with a diagnosis of MDD (ie, a score of 13^{17}). It has previously been observed that improvements on functional outcome measures may lag behind the changes in core symptoms of depression assessed with depressive ratings scales; therefore, a period of more than 8 weeks may be required before the full extent of improvement can be fully assessed.^{34–36} Thus, it is likely that a greater degree of improvement may have been seen if the treatment duration had been more than 8 weeks. The observed improvements in functional outcomes in patients with MDD, including improvements in work, social, and family activities and the patient's overall outlook and interest in life events, are significant, but longer trials may be required to more fully assess the effect of desvenlafaxine on improving functional impairment.

The results of the predictor analysis suggest that the treatment effect of desvenlafaxine compared with placebo increased as patients become more functionally impaired and decreased as well-being baseline increased. In addition, younger age and Hispanic race/ethnicity were found to be Figure 6. MADRS Lassitude Item Change From Baseline Scores With Desvenlafaxine (LOCF); ITT Population^a



^aAnalysis of the MADRS is based on the 9-study, pooled population. ^bPlacebo values are based on the total pooled population. *P* values are based on individual-dose comparisons with their respective placebo groups.

*P < .05 desvenlafaxine 50 and 400 mg/d versus placebo.

**P<.01 desvenlafaxine 50, 100, 200, and 400 mg/d versus placebo.

Abbreviations: ITT = intent to treat, LOCF = last observation carried

forward, MADRS = Montgomery-Asberg Depression Rating Scale.

predictive of improvements on the SDS and WHO-5, respectively. These predictors are of interest and deserve further investigation. One could speculate that the psychosocial impairments of younger patients may be less entrenched than those experienced by older patients and therefore younger patients may experience more rapid benefits of treatment (ie, within 8 weeks) in terms of overall functioning and well-being. However, few similar analyses have been conducted to date, so any extrapolation of these results to other populations is cautioned. Future research is needed to further explore this relationship and to quantify the correlation between improvements in functional impairment and depressive symptomatology in various subpopulations of patients with MDD.

CONCLUSION

Short-term treatment with desvenlafaxine was associated with greater improvement compared with placebo with respect to work, family functioning and social functioning, and overall well-being in patients with MDD.

Drug names: desvenlafaxine (Pristiq), duloxetine (Cymbalta), paroxetine (Paxil, Pexeva, and others), venlafaxine (Effexor and others). Author affiliations: Department of Psychiatry and Behavioural Neurosciences, Mood Disorders Division, McMaster University, Hamilton, Ontario, Canada (Dr Soares); Department of Psychiatry, Mood Disorders Institute, Virginia Commonwealth University, Richmond (Dr Kornstein); Department of Psychiatry, University of Pennsylvania School of Medicine, Philadelphia (Dr Thase); and Wyeth Research, Collegeville, Pennsylvania (Dr Guico-Pabia and Ms Jiang). Financial disclosure: Dr Soares has received grant/research support from Eli Lilly, AstraZeneca, Physicians Services Incorporated (PSI) Foundation, Allergen National Centre of Excellence, Hamilton Community Foundation, Lundbeck, Wyeth, and Canadian Institute of Health Research; has been a research consultant for Wyeth, Lundbeck, and Bayer; and has served on speakers' bureaus or advisory boards for AstraZeneca, Wyeth, and Bayer. Dr Kornstein has received grant/ research support from US Department of Health and Human Services, National Institute of Mental Health, Bristol-Myers Squibb, Pfizer, Eli Lilly, Forest, Wyeth, Novartis, Sepracor, Boehringer-Ingelheim, Sanofi-Aventis, AstraZeneca, and Takeda; has served on advisory boards for Wyeth, Pfizer, Eli Lilly, Forest, Sepracor, Takeda, and Endo; and has received book royalties from Guilford Press. Dr Thase has been an advisor/consultant to AstraZeneca, Bristol-Myers Squibb, Eli Lilly, Forest, GlaxoSmithKline, Janssen, MedAvante, Neuronetics, Novartis, Schering-Plough, Shire, Supernus, Transcept, and Wyeth; has received grant support from Eli Lilly, GlaxoSmithKline, the National Institute of Mental Health, and Sepracor; has been on the speakers bureau for AstraZeneca, Bristol-Myers Squibb, Eli Lilly, and Wyeth; holds equity in MedAvante; receives royalties from American Psychiatric Publishing, Guilford Publications, Herald House, and W.W. Norton. Dr Thase's spouse is an employee of Advogent. Dr Guico-Pabia and Ms Jiang are employees of Wyeth.

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