ORIGINAL RESEARCH

Key Words: Care management, Dialogues program, primary care, venlafaxine ER, major depressive disorder

Patient Outcomes With Education, Drug Therapy, and Support: A Study of Venlafaxine ER-Treated Outpatients with Major Depressive Disorder

By Kasia Lobello, Sujana Reddy, Jeff Musgnung, Ronald Pedersen, Philip T. Ninan

ABSTRACT ~ Objective: *Dialogues Time to Talk (Dialogues) is a care management program that provides additional follow-up care and patient education for outpatients with major depressive disorder (MDD) starting venlafaxine extended release (ER) therapy. This study examined the effect of the Dialogues program on patient treatment satisfaction.* ***Methods:*** *In this 6-month, open-label study, primary care patients with MDD received usual care and were randomly assigned to venlafaxine ER (75 to 225 mg/d) either alone or in combination with the Dialogues program (venlafaxine ER + D). The primary outcome was patient treatment satisfaction on day 112, measured by the 10-point Satisfaction with Depression Care Scale (SDCS). Secondary efficacy outcomes included the 17-item Hamilton Rating Scale for Depression (HAM-D_{17}) total score, response (≥50% decrease from baseline HAM-D_{17} score), and remission (HAM-$D_{17} \leq 7$).* ***Results:*** *The modified intent-to-treat population included 263 patients in the venlafaxine ER group and 257 in the venlafaxine ER+D group. The percentage of patients with an SDCS "very satisfied" score (≥8) at day 112 was not significantly different in the venlafaxine ER and venlafaxine ER+D groups (63% and 58%, respectively; P = 0.22). No significant differences were found on any secondary outcomes.* ***Conclusion:*** *Among primary care patients starting venlafaxine ER for MDD, participation in the Dialogues program did not have a statistically significant effect on patient treatment satisfaction.* Psychopharmacology Bulletin. *2010;43(2):24–40.*

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INTRODUCTION

Major depressive disorder (MDD) is among the most common mental health disorders seen in primary care settings, yet it is frequently underdiagnosed and inadequately treated.[2–4] Among patients who receive treatment for MDD, approximately 45% are treated in a primary care setting and 55% are treated in a psychiatric setting.[5] An estimated 75% of depressed patients in primary care do not receive an effective level of treatment with psychotherapy or antidepressants and only one third receive any psychotherapy.[4] Furthermore, few primary care patients treated with antidepressants receive adequate follow-up care, and only half receive 3 months of adequate antidepressant treatment.[6]

Obstacles to treatment success in primary care include factors related to the medication, the patient, or the clinician, and may include lack of efficacy, anticipated or actual adverse events (AEs), fear of drug dependence, and the stigma associated with mental illness.[7] Additionally, clinicians may be limited by time constraints and a lack of resources.[8] All of these factors may reduce patient satisfaction and discourage patients from maintaining therapy. Primary care treatment programs that provide follow-up care and patient education without placing additional strains on clinician resources are likely to improve treatment success and patient satisfaction. The introduction of a care management program in addition to usual care has been shown, albeit inconsistently, to help overcome obstacles to adequate depression treatment in primary care settings and to enhance the quality of patient care.[9–13]

The Dialogues Time to Talk program (Dialogues; Table 1) is a care management tool initiated by Wyeth Pharmaceuticals and designed for patients with MDD who are starting therapy with venlafaxine extended release (ER). Dialogues was launched in the United States in 2005 and has since expanded to become a multilingual, international program providing support to patients and physicians in multiple countries.

The Dialogues program is designed to improve patients' and families' understanding of MDD and its treatment and to provide supportive messages for patients and encourage them to play an active role in managing their condition. The program emphasizes that the goal of depression care is to achieve remission during the first 6 to 8 weeks of therapy and to maintain remission and prevent relapse during the next 16 to 20 weeks of therapy. Further, Dialogues urges that patients should not be satisfied with treatment until they achieve remission, with depressive symptoms virtually eliminated. The program aims to help patients achieve successful outcomes by reinforcing physician treatment efforts, providing feedback to treating physicians, and encouraging better doctor-patient communication.

TABLE 1

DIALOGUES PROGRAM FLOWCHART

WEEK OF PARTICIPATION IN DIALOGUES PROGRAM	TYPE OF PATIENT SUPPORT
0	Welcome kit: *Dialogues Magazine*, issue 1 *Straight Talk on Side Effects* booklet Tip card of key points for discussion with the physician
1	Phone call from registered nurse to patient
3	Dialogues resource guide
5	Phone call from registered nurse to patient
6	*Dialogues Magazine*, issue 2 *Straight Talk on Progress* booklet
12	*Dialogues Magazine*, issue 3 *Straight Talk on Managing Stress* booklet
13	Phone call from registered nurse to patient
16	*Straight Talk on Long-Term Therapy* booklet

A 6-month, open-label study, "Patient Outcomes with Education, Drug Therapy, and Support" (POETS), evaluated the Dialogues program among primary care patients with MDD. The primary objective of the POETS study was to examine the effect of Dialogues on patient satisfaction with depression treatment. Secondary objectives included comparisons of the proportion of patients who completed the study and the time to discontinuation in each treatment group. Additional objectives included comparisons of remission rates, outcome measures indicative of patient functioning, and safety between treatment groups.

METHODS

The POETS study was a phase 4, 6-month, randomized, open-label, multicenter trial conducted from June 2006 to October 2007 in the United States in 45 primary care centers. The protocol received institutional review board approval before the study began. The study was conducted in accordance with the ethical principles in the Declaration of Helsinki, and was designed and performed in compliance with Good Clinical Practice. All participants provided written informed consent before enrollment.

Patients

Eligible participants were male and female outpatients aged 18 years or older with a primary diagnosis of MDD. At screening, a psychiatric assessment was performed by the investigator (ie., the patient's primary

care physician) using a modified Mini-International Neuropsychiatric Interview, and a diagnosis of MDD—single or recurrent episode without psychotic features—was confirmed according to *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV)[14] criteria. Patients were required to have a minimum 17-item Hamilton Rating Scale for Depression ($HAM\text{-}D_{17}$)[15] total score of 14. Sexually active women of child bearing potential were required to use medically acceptable contraception.

Major exclusion criteria included current treatment with venlafaxine or previously failed venlafaxine treatment at adequate dose and duration; significant risk of suicide based on clinical judgment; pregnancy or breastfeeding; introduction or change in cognitive behavioral therapy, interpersonal therapy, or other psychotherapy within 3 months before randomization; and concomitant use of other psychopharmacologic drugs.

Study Design

On study day 1 (baseline visit), after baseline assessments, eligible participants were randomly assigned into 1 of 2 treatment regimens: venlafaxine ER or venlafaxine ER plus Dialogues (ER+D). Patients randomly assigned to the venlafaxine ER group received venlafaxine ER as part of the standard practice of care for the treatment of MDD, as determined by the investigator. Patients randomly assigned to the venlafaxine ER+D group received venlafaxine ER treatment plus the Dialogues program, as part of the standard practice of care for the treatment of MDD as determined by the investigator.

All patients were started on venlafaxine ER therapy no later than 2 days after the baseline visit. Patients were assessed on days 14, 45, 112, 135, and 180. Any patient who discontinued from the study before day 180 had early discontinuation assessments performed as soon as possible after treatment discontinuation. The visit window was ± 3 days for the day 14 visit, and ± 5 days for the visits scheduled on days 45 through 180. Additional visits (eg., dose adjustment) were scheduled at the discretion of the investigator.

Venlafaxine ER Treatment

Venlafaxine ER was supplied by a retail pharmacy of the patient's choice and all patients were given a prescription copay reduction card at randomization that provided venlafaxine ER at no charge. Regardless of treatment group assignment, venlafaxine ER dosage for each patient was determined by the investigator, in accordance with the dosage and administration guidelines per the product label. In general, the dosing

strategy was to start patients on the lowest effective dose of venlafaxine ER (75 mg/d). For a patient who did not respond to the initial 75-mg/d dose, it could be increased to a maximum of 225 mg/d. At any time during the study, a patient's dose could be increased or decreased at the investigator's discretion.

The Dialogues Program

As shown in Table 1, patients in the Dialogues program received a welcome kit upon enrollment that included the first issue of the *Dialogues Magazine*, a *Straight Talk* booklet, and a tip sheet. Over a 4-month period, patients also received a comprehensive resource guide, 2 additional issues of the *Dialogues Magazine*, and 3 additional *Straight Talk* booklets. Patients also received 3 planned periodic calls from a registered nurse and had access to a 12-hour daily help line. After each telephone call with a patient, a contact report was sent to the treating clinician.

Efficacy and Safety Assessments

The primary efficacy measure was patient treatment satisfaction on study day 112, which was evaluated by the Satisfaction with Depression Care Scale (SDCS), a 10-point, patient-rated, visual analog scale designed to assess patient satisfaction with depression care. SDCS scores ranged from 0 (not at all satisfied) to 10 (extremely satisfied), and patients were asked to circle the number indicating how satisfied they had been with their depression care over approximately the last week. A response of "very satisfied" was defined as an SDCS score $\geq$8. The SDCS was assessed at all scheduled study visits, except for the baseline (day 1) visit.

Investigator-assessed secondary efficacy measures included the HAM-D_{17}, the Clinical Global Impressions–Improvement (CGI-I) scale,[16] and the Clinical Global Impressions–Severity (CGI-S) scale.[16] HAM-D_{17} remission was defined as a total score $\leq$7 and HAM-D_{17} response was defined as a $\geq$50% reduction from baseline. CGI-I scores were rated from 1 (very much improved) to 7 (very much worse), and CGI-I response was defined as a score $\leq$2 (very much improved/much improved). CGI-S scores were rated from 1 (normal, not at all ill) to 7 (among the most extremely ill patients) and CGI-S response was defined as a score $\leq$2 (normal, not at all ill/borderline mentally ill). Patient-rated secondary efficacy measures included the Patient Global Impressions–Improvement Scale (PGI-I),[16] Patient Global Impressions–Severity (PGI-S),[16] and Inventory for Depressive Symptomatology–Self-Report (IDS-SR).[17] PGI-I scores

were rated from 1 (very much improved) to 7 (very much worse); PGI-I response was defined as a score ≤2 (very much improved/much improved). The secondary efficacy measures, with the exception of the CGI-I and the PGI-I, were completed at baseline and during all scheduled study visits (days 14, 45, 112, 135, and 180). The CGI-I and PGI-I were not administered at baseline. Health outcomes assessments used in the study included 3 patient-rated items: the Sheehan Disability Scale (SDS),[18] the WHO 5-Item Well Being Index (WHO-5),[19] and the Medication Adherence Questionnaire (MAQ).[20] MAQ responders were defined as never missing a dose of medication. Patients completed the SDS and the WHO-5 at every scheduled study visit and the MAQ at every scheduled study visit with the exception of baseline.

Safety was monitored by reports of AEs at all visits and the following vital sign measurements: height (baseline only), weight (baseline and study day 180), resting pulse rate, 2 sitting blood pressure readings (baseline and study days 14, 45, 112, 135, and 180), and physical examinations (baseline and study day 180). Additional visits were permitted for safety reasons or to evaluate loss of efficacy.

Statistical Analysis

The efficacy analyses were conducted using the modified intent-to-treat (mITT) population, which included all patients who were prescribed venlafaxine ER and had at least one postbaseline efficacy evaluation. Patients who were given study medication but for whom it was not known whether the medication was taken were assumed to be treated. The primary efficacy end point, the proportion of patients with a response of "very satisfied" on the SDCS (score ≥8) on study day 112, was compared between treatment groups using the Cochran-Mantel-Haenszel (CMH) procedure, stratified by pooled study center. Center pooling was based on the observed distribution of the number of subjects enrolled at each center before data base lock. For patients who discontinued treatment in any interval between the scheduled visits, a final assessment was obtained as soon as possible after treatment was discontinued. If a final assessment could not be made (ie., patient lost to follow-up), the last observed score was carried forward. All efficacy values obtained >3 days after the last day of treatment were excluded. Although this excludes data from a number of patients, this definition is consistent with the definition of final on-therapy in the studies that supported the approval of venlafaxine ER for the treatment of MDD.

The proportion of patients who completed the study (6 months) was analyzed using the CMH procedure. In addition, the time to discontinuation was analyzed using the log-rank test. Dichotomous outcomes

(eg., HAM-D_{17} response) were analyzed using the CMH procedure, stratified by pooled study center. Continuous measures where a baseline value was available were analyzed using a 2-way analysis of covariance (ANCOVA) model with pooled center and treatment as factors and baseline value as the covariate. An analysis of variance (ANOVA) model with effects for pooled center and treatment were used to analyze continuous measures with no baseline value (ie., CGI-I and PGI-I). All statistical tests were 2-sided with an alpha level of ≤ 0.05.

RESULTS

Patients

The study enrolled 537 patients; 269 patients were randomly assigned to the venlafaxine ER group and 268 to the venlafaxine ER+D group (Figure 1). During the on-therapy period, a total of 209 (39%) patients discontinued from the study, 97 (36%) from the venlafaxine ER group and 112 (42%) from the venlafaxine ER+D group; discontinuations by primary reason are shown for each group in Figure 1. AEs were a primary reason for discontinuation in 34 (13%) patients in the venlafaxine ER group and 45 (17%) patients in the venlafaxine ER+D group. Time to discontinuation due to AEs was not significantly different between treatment groups (log-rank test, $P = 0.45$). The mITT population comprised 520 patients who were evaluated for efficacy, including 263 patients in the venlafaxine ER group and 257 in the venlafaxine ER+D group. There were no significant differences among treatment groups in pretreatment demographic and clinical characteristics (Table 2).

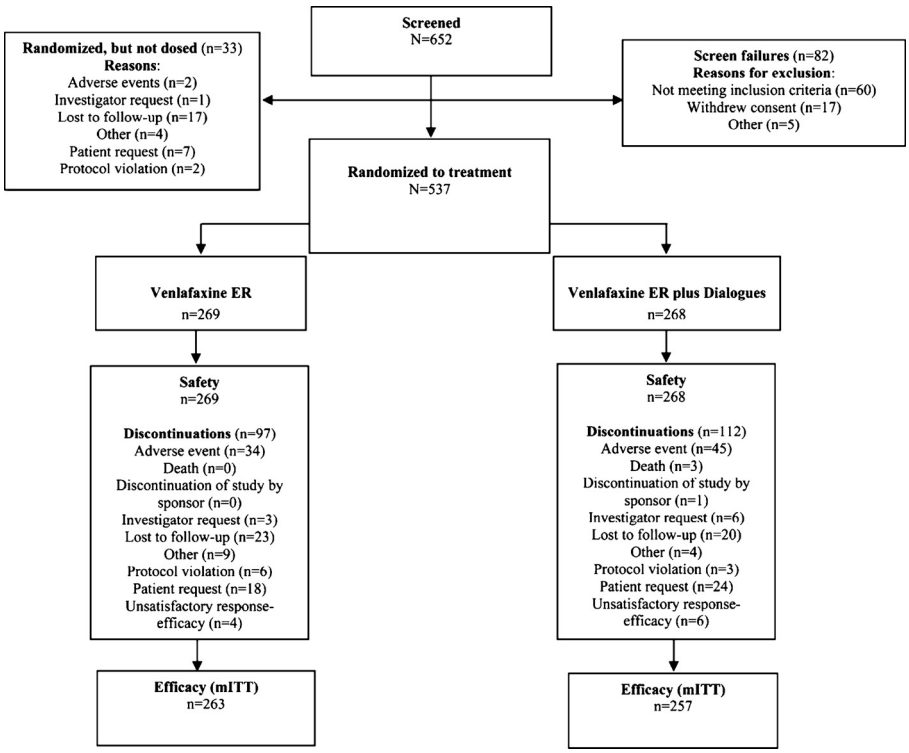
Efficacy Evaluation

Results for the primary efficacy end point are presented in Table 3. The percentage of patients with an SDCS score of "very satisfied" (score ≥ 8) at study day 112 was not significantly different in the venlafaxine ER and venlafaxine ER+D groups (63.0% and 57.7%, respectively; $P = 0.22$). At the study day 112 evaluation, adjusted mean scores on the SDCS were 7.61 for the venlafaxine ER group and 7.56 for the venlafaxine ER+D groups; the difference between groups was not statistically significant ($P = 0.82$; Table 4).

Results of secondary efficacy measures were similar to the pattern observed with the primary efficacy measure and are shown in Tables 3 and 4. No significant differences were observed between the venlafaxine ER and venlafaxine ER+D groups in the percentages of patients

FIGURE 1

POETS ANALYSIS POPULATION



Abbreviations: mITT, modified intent to treat; POETS, Patient Outcomes with Education, Drug Therapy, and Support study.

who attained HAM-D_{17} remission (62.9% vs 60.3%, respectively; $P = 0.49$), HAM-D_{17} response (72.7% vs 68.2%, respectively; $P = 0.24$), CGI-I response (73.9% vs 72.8%, respectively; $P = 0.65$), CGI-S response (64.4% vs 63.2%, respectively; $P = 0.59$), and PGI-I response (75.2% vs 74.5%, respectively; $P = 0.95$). Additionally, a similar percentage of patients in the venlafaxine ER and venlafaxine ER+D groups reported never missing a dose of medication on the MAQ (97.6% vs 98.3%, respectively; $P = 0.56$).

Changes from baseline to the LOCF end point for additional secondary efficacy measures and patient-reported health outcomes are presented in Table 4. Results of these measures also were similar to the pattern observed with the primary efficacy measure, with no significant differences reported between treatment groups. At the last-observation-carried-forward (LOCF) day 180 evaluation, adjusted mean changes

TABLE 2

DEMOGRAPHIC AND BASELINE CHARACTERISTICS, mITT POPULATION

CHARACTERISTIC	VENLAFAXINE ER (75 TO 225 MG/D) (N = 263)	VENLAFAXINE ER (75 TO 225 MG/D) PLUS DIALOGUES (N = 257)
Age, mean (SD), years	44 (14)	45 (14)
Sex, n (%)		
Female	196 (75)	181 (70)
Male	67 (25)	76 (30)
Race, n (%)		
White	230 (87)	224 (87)
Black	26 (10)	25 (10)
Other	7 (3)	8 (3)
Weight, mean (SD), kg	87 (22)	90 (23)
Duration of current episode, mean (SD), months	25 (55)	20 (48)
HAM-D_{17} total score, mean (SD)	20 (4)	20 (4)
CGI-S score		
Moderately ill, n (%)	161 (62)	157 (61)
Markedly ill, n (%)	67 (26)	51 (20)
Severely ill, n (%)	7 (3)	9 (4)

Abbreviations: CGI-S, Clinical Global Impressions–Severity Scale; ER, extended release; HAM-D_{17}, 17-item Hamilton Rating Scale for Depression; mITT, modified intent to treat; SD, standard deviation.

from baseline in the venlafaxine ER and venlafaxine ER+D groups were similar for HAM-D_{17} total scores (−12.18 for both groups $P = 0.99$), IDS-SR total scores (−20.45 vs −19.41, respectively; $P = 0.32$), PGI-S scores (−1.95 vs −1.90, respectively; $P = 0.67$), SDS total scores (−8.97 vs −8.48, respectively; $P = 0.45$), and WHO-5 total scores (8.38 vs 8.20, respectively; $P = 0.72$). The adjusted mean HAM-D_{17} total scores over time (LOCF) are illustrated in Figure 2.

Safety Evaluation

There were no major differences between the 2 treatment groups with regard to the percentage of patients who withdrew from the study due to AEs or who experienced treatment-emergent AEs (TEAEs) during the on-therapy period. Of the 537 patients in the study, 83 (16%) withdrew because of AEs (as a primary or secondary reason) during the on-therapy period including 35 (13%) patients from the venlafaxine ER group and 48 (18%) patients from the venlafaxine ER+D group. (These numbers differ from those in Figure 1, which presents the primary reasons for discontinuation.) A total of 423 patients experienced

TABLE 3

PRIMARY AND SECONDARY EFFICACY OUTCOMES AT THE LOCF END POINT, mITT POPULATION

OUTCOME MEASURE/TREATMENT GROUP	LOCF END POINT ANALYSIS, % (N/TOTAL N)	*P* VALUE VS VENLAFAXINE ER
Primary efficacy measure		
SDCS "Very Satisfied" score,[a] day 112		
Venlafaxine ER	63.0 (160/254)	
Venlafaxine ER plus Dialogues	57.7 (138/239)	0.22
Secondary efficacy measures		
HAM-D_{17} remission,[b] day 180		
Venlafaxine ER	62.9 (159/253)	
Venlafaxine ER plus Dialogues	60.3 (144/239)	0.49
HAM-D_{17} response,[c] day 180		
Venlafaxine ER	72.7 (184/253)	
Venlafaxine ER plus Dialogues	68.2 (163/239)	0.24
CGI-I response,[d] day 180		
Venlafaxine ER	73.9 (187/253)	
Venlafaxine ER plus Dialogues	72.8 (174/239)	0.65
CGI-S response,[e] day 180		
Venlafaxine ER	64.4 (163/253)	
Venlafaxine ER plus Dialogues	63.2 (151/239)	0.59
PGI-I response,[f] day 180		
Venlafaxine ER	75.2 (191/254)	
Venlafaxine ER plus Dialogues	74.5 (178/239)	0.95
MAQ response,[g] day 180		
Venlafaxine ER	97.6 (248/254)	
Venlafaxine ER plus Dialogues	98.3 (235/239)	0.56

Abbreviations: CGI-I, Clinical Global Impressions–Improvement Scale; CGI-S, Clinical Global Impressions–Severity Scale; ER, extended release; HAM-D_{17}, 17-item Hamilton Rating Scale for Depression; LOCF, last observation carried forward; MAQ, Medication Adherence Questionnaire; mITT, modified intent to treat; PGI-I, Patient Global Impressions–Improvement Scale; SDCS, Satisfaction with Depression Care Scale.

[a]SDCS "very satisfied" score was defined as score ≥8.

[b]HAM-D_{17} remission was defined as total score ≤7.

[c]HAM-D_{17} response was defined as ≥50% decrease from baseline.

[d]CGI-I response was defined as score of 1 (very much improved) or 2 (much improved).

[e]CGI-S response was defined as score of 1 (normal, not at all ill) or 2 (borderline mentally ill).

[f]PGI-I response was defined as score of 1 (very much improved) or 2 (much improved).

[g]MAQ response was defined as never missing a dose of medication.

TEAEs, 209 (78%) patients in the venlafaxine ER group and 214 (80%) in the venlafaxine ER+D group. The most common TEAEs (incidence of at least 10%) in the venlafaxine ER group were insomnia (36, 13%), headache (30, 11%), and nausea (27, 10%). The most common TEAEs in the venlafaxine ER+D group were nausea (42, 16%), insomnia (38, 14%), and constipation (34, 13%). Overall, TEAEs were consistent with those observed with the SNRI class,[21] as well as with previous trials of venlafaxine ER.[22,23]

TABLE 4

Changes From Baseline to LOCF End Point for Selected Secondary Efficacy Outcomes, mITT Population

Outcome measure/treatment group	N	Baseline raw mean score*	Adjusted mean change† (SE)	Difference in adjusted means (95% CI)	*P* value vs venlafaxine ER
SDCS, day 112					
Venlafaxine ER	254	6.90	7.61 (7.33, 7.89)		
Venlafaxine ER plus Dialogues	239	7.04	7.56 (7.27, 7.85)	0.048 (−0.36, 0.45)	0.82
HAM-D_{17} total score, day 180					
Venlafaxine ER	253	19.62	−12.18 (0.39)		
Venlafaxine ER plus Dialogues	239	19.69	−12.18 (0.40)	0.01 (−1.09, 1.11)	0.99
IDS-SR total score, day 180					
Venlafaxine ER	254	39.18	−20.45 (0.72)		
Venlafaxine ER plus Dialogues	239	38.00	−19.41 (0.75)	−1.03 (−3.07, 1.01)	0.32
PGI-S score, day 180					
Venlafaxine ER	254	4.16	−1.95 (0.08)		
Venlafaxine ER plus Dialogues	239	4.05	−1.90 (0.09)	−0.05 (−0.29, 0.18)	0.67
SDS total score, day 180					
Venlafaxine ER	254	17.16	−8.97 (0.46)		
Venlafaxine ER plus Dialogues	238	16.56	−8.48 (0.47)	−0.49 (−1.78, 0.79)	0.45
WHO-5 total score, day 180					
Venlafaxine ER	254	6.23	8.38 (0.37)		
Venlafaxine ER plus Dialogues	239	6.76	8.20 (0.38)	0.19 (−0.85, 1.22)	0.72

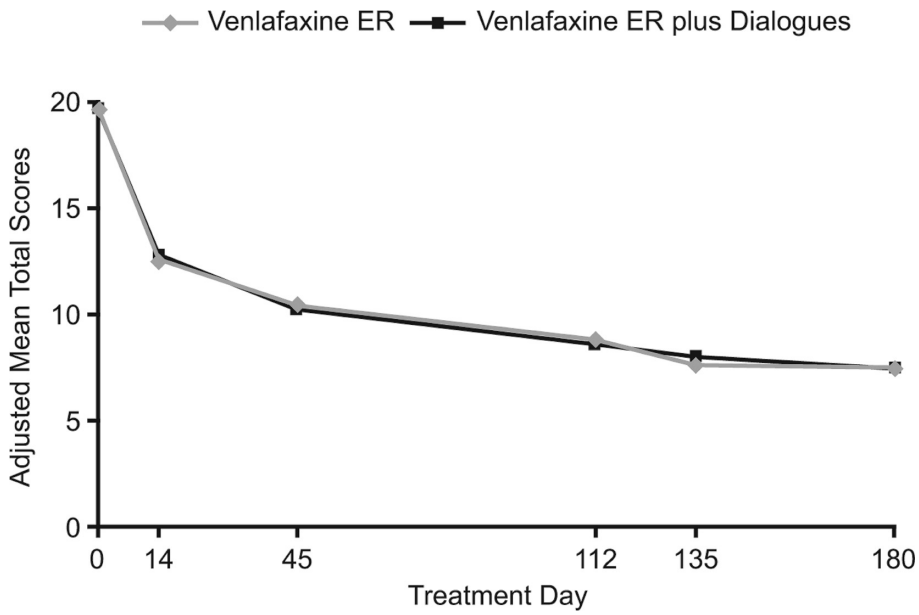
Abbreviations: CI, confidence interval; ER, extended release; HAM-D_{17}, 17-item Hamilton Rating Scale for Depression; IDS-SR, Inventory for Depressive Symptomatology–Self-Report; mITT, modified intent to treat; LOCF, last observation carried forward; PGI-S, Patient Global Impressions–Severity; SDCS, Satisfaction with Depression Care Scale; SDS, Sheehan Disability Scale; SE, standard error; WHO-5, World Health Organization 5-Item Well-Being Index.

*Day 14 score shown for SDCS.

†Adjusted means and 95% CI shown for SDCS.

FIGURE 2

POETS STUDY: HAM-D_{17} ADJUSTED MEAN TOTAL SCORES OVER TIME, LOCF, mITT POPULATION



Abbreviations: ER, extended release; HAM-D_{17}, 17-item Hamilton Rating Scale for Depression; LOCF, last observation carried forward; mITT, modified intent to treat; POETS, Patient Outcomes with Education, Drug Therapy, and Support study.
Note: No significant differences were observed between treatment groups at any time point.

Venlafaxine ER treatment in both groups was associated with few clinically important changes in vital signs, body weight, and physical examination findings.

Of the 537 patients in the safety population, 29 (5%) patients had 1 or more serious AEs. Three (0.6%) patients died during the study; all were from the venlafaxine ER+D group. The events leading to death were coronary atherosclerosis, intracranial hemorrhage, and suicide. The investigators considered the coronary atherosclerosis and intracranial hemorrhage not related to the study drug or study protocol. The suicide was considered as possibly related to the study drug by the investigator, though the medical monitor judged it not related.

DISCUSSION

In the POETS study, participation in the Dialogues program did not have a statistically significant effect on any of the efficacy end points in the study, as compared with venlafaxine ER treatment alone. On the primary efficacy measure, the percentage of patients with an SDCS

score of "very satisfied" improved over the course of the study in both groups but was not significantly different between treatment groups at day 112. Results of the secondary efficacy measures were similar to the pattern observed on the primary efficacy measure, with no significant differences observed between treatment groups. Venlafaxine ER appeared efficacious in both treatment groups. Time to discontinuation, overall discontinuation rates, and discontinuations due to AEs also did not differ significantly between groups.

Although it is unclear why the Dialogues program had a nonsignificant effect on treatment satisfaction, the finding may be related to study methodology. The Dialogues program encouraged patients to demand more from their care, that is, not to be satisfied with treatment until they were virtually symptom-free. As a result, patients in the Dialogues program may have had higher expectations for treatment success and therefore a lesser degree of satisfaction with treatment compared with patients not randomized to the program. Furthermore, regardless of treatment assignment, all patients in the study received extra attention from their providers (physician/investigator and other health care professionals) as compared to medical care in a nonstudy setting. This additional time and attention, such as time spent completing rating scales and the frequent study visits, may have improved treatment satisfaction and medication adherence in both groups, diluting any benefits that may have been gained from the Dialogues program. Dialogues may be more helpful in a "real world" primary care setting, in which time with clinicians is more limited and the program provides additional follow-up care and patient education. The lack of separation between treatment groups in the study may also be due in part to the overall positive response to venlafaxine ER therapy, which was shown to be efficacious across depression-related outcome measures in both treatment groups. Patients receiving highly effective pharmacologic therapy may be less likely to benefit from patient support programs.

The lack of significant differences between the usual care and Dialogues groups in this study is generally consistent with previous findings by Perahia et al[24] and Simon et al.[25] Perahia and colleagues found that combining antidepressant medication with a psychoeducational telephone intervention did not improve depression outcomes compared with antidepressant medication alone. Outpatients with MDD in primary and psychiatric practice settings were randomly assigned to open-label duloxetine either alone (n = 485) or in combination with a telephone intervention (n = 477) for 12 weeks. The telephone intervention was designed to provide information about MDD and consisted of 3 calls over 12 weeks delivered by a health care professional. At study end point,

remission rates and all secondary outcomes were similar between groups, as were the percentage of patients who completed the study, discontinuation rates due to AEs, and adherence to medication. However, the telephone intervention was associated with increased reporting of AEs. The authors speculated that the lack of significant differences in depression outcomes between groups may have been due to the high drug adherence in both treatment groups and suggested that further study was warranted in a more naturalistic clinical setting.[26]

Simon and colleagues[25] also found that a low-intensity telephone care management program offered no significant advantage over usual care for patients with MDD who were starting antidepressant treatment. In the study, eligible patients in a prepaid health plan receiving new antidepressant prescriptions from psychiatrists were randomly assigned to continued usual care (n = 104) or to a 3-session telephone care management program (n = 103). Care management contacts included assessment of depressive symptoms, medication adherence, and medication side effects with structured feedback from psychiatrists. Compared with usual care, the care management program had no significant effect on mean depression scores at 6 months, the probability of patient-rated improvement, or medication adherence over 6 months.[25]

On the other hand, results of several randomized, controlled trials of depressed patients in primary care have shown that the addition of telephone care management programs to antidepressant treatment improves clinical outcomes and quality of patient care.[9–13] Patient self-rated reports regarding quality of care showed greater patient satisfaction with telephone care management and pharmacotherapy than with pharmacotherapy alone.[9,12] In addition, the care management interventions resulted in greater improvement in depressive symptoms[9,11–13] and increased medication adherence[11–13] compared with antidepressant treatment alone. The dissimilarity in results of these trials and the current study may be due in part to differences in the patients studied, the intensity and design of the care management programs, or in the usual care treatment administered to patients.

Strengths and Limitations

The strengths of the study include its large sample size and randomized design, the broad range of efficacy measures used, and the flexible-dose treatment schedule, which reflects "real life" medical practice. Certain limitations related to study design merit consideration. Interpretation of the results is limited by the open-label design and the use of inclusion and exclusion criteria, which like most clinical trials, may have resulted in a patient sample that is not representative of

patients in clinical practice. Also, like most clinical trials, the frequency of study visits and use of standardized assessment scales are not common in typical primary care treatment settings, and as such, the results may not be broadly generalizable to clinical practice. Another weakness of the study is that there was no confirmation as to whether or not patients randomly assigned to the Dialogues group actually took advantage of the materials provided.

With respect to the non-significant study results on the primary outcome measure, assessments with the SDCS relied on patient recall and, in retrospect, the scale may have been too general to adequately ascertain the role of the Dialogues program in determining patient satisfaction with depression care. As noted earlier, SDCS scores for patients in the Dialogues group may have been negatively affected by higher expectations for treatment outcomes while scores for patients in both groups may have reflected positive effects of non-specific study design factors on treatment satisfaction to a degree that overshadowed any potential benefits from the program. As such, the full benefits of Dialogues or similar programs may be more readily demonstrated in a setting that more closely mirrors clinical practice where time and resources are considerably more limited.

The non-significant results of this study add to a somewhat inconsistent body of literature regarding the benefits of programs intended to improve patient care and highlight some of the challenges inherent in attempting to determine the value of such programs. Although the nature of clinical studies limits the generalizability of the results, there exists a need for an evidence base for making decisions about the implementation of programs like Dialogues. In that context, the results of studies that do not demonstrate a significant effect of the addition of programs designed to improve quality of care, treatment outcomes, or patient satisfaction, while somewhat disappointing, are nonetheless important to inform clinical practice.

CONCLUSIONS

This clinical trial failed to demonstrate a statistically significant advantage of the Dialogues program over usual care in patients receiving treatment with venlafaxine ER for MDD in a primary care setting. Venlafaxine ER appeared efficacious in patients receiving either usual care or the Dialogues program in addition to usual care. Dialogues provides additional follow-up care and patient education that may be more helpful in a "real world" primary care setting, in which time with the clinician is more limited than in a clinical study. ✤

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