

The RECONNECT Study: Effectiveness of Vortioxetine (10–20 mg/day) in Patients With Major Depressive Disorder Comorbid With Generalized Anxiety Disorder

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BACKGROUND

- Major depressive disorder (MDD) and generalized anxiety disorder (GAD) are frequently comorbid; individuals experiencing comorbid GAD represent one of the largest patient groups within MDD^{1–3}
- Patients with comorbid MDD and GAD are difficult to treat. When comorbid, these conditions are associated with more severe symptoms, greater impairment in functioning and health-related quality of life (HRQoL), longer treatment duration, and lower remission rates^{1,2,4}
- Vortioxetine is effective and well tolerated for the treatment of depressive symptoms and cognitive deficits in patients with MDD.⁵ Vortioxetine has anxiolytic effects in patients with MDD experiencing severe anxiety symptoms,^{6,7} and has been shown to be effective for the relief of anxiety symptoms in patients with GAD^{8,9}

PURPOSE

- This study was undertaken to assess the effectiveness of vortioxetine in patients with MDD comorbid with GAD

METHODS

- An open-label, 8-week, multicenter study in outpatients aged 18–65 years (NCT04220996)
- Inclusion criteria:
 - Diagnostic and Statistical Manual of Mental Disorders-5 diagnosis of MDD and comorbid GAD (made before the current major depressive episode [MDE])
 - Duration of current MDE <12 months
 - Montgomery-Åsberg Depression Rating Scale (MADRS) total score ≥22
 - Hamilton Anxiety Rating Scale (HAM-A) total score ≥20
- Patients were receiving vortioxetine as a first treatment for the current MDE or switching to vortioxetine due to inadequate response to another antidepressant
- Starting dose of vortioxetine was 10 mg/day, to be increased to 20 mg/day in all patients after 1 week per the study protocol (subsequent dose reductions permitted based on individual tolerability/response)
- Clinician assessments: MADRS, HAM-A, Clinical Global Impression-Severity (CGI-S), and Functioning Assessment Short Test (FAST)
 - Response: ≥50% decrease in MADRS or HAM-A total score from baseline
 - Remission: MADRS or HAM-A total score ≤10 at week 8
- Patient assessments: Hospital Anxiety and Depression Scale (HADS) and Quality of Life Enjoyment and Satisfaction Questionnaire (long form) [Q-LES-Q (LF)]
- Primary study endpoint was change from baseline to week 8 in MADRS total score
- For all endpoints reported, least squares mean change from baseline was estimated using a mixed model for repeated measurements with week and site as fixed factors and baseline score as a covariate. The interaction between week and baseline total score was included in the model, and an unstructured covariance matrix was applied

RESULTS

Study Population

- Of the 100 patients treated in the study (Table 1), 77 were switching to vortioxetine due to inadequate response to prior therapy (mostly selective serotonin reuptake inhibitors, n=58)

Table 1. Patient Demographics and Disease Characteristics at the Start of Vortioxetine Treatment

	First Treatment	Switch	Total
Demographic characteristics			
Patients, n	23	77	100
Age (years), mean ± SD	39.1 ± 12.5	43.1 ± 10.6	42.2 ± 11.1
Female, n (%)	13 (56.5)	50 (64.9)	63 (63.0)
White, n (%)	14 (60.9)	65 (84.4)	79 (79.0)
Features of current MDE			
Duration (weeks), mean ± SD	13.6 ± 10.4	15.7 ± 9.1	15.2 ± 9.4
First MDE, n (%)	0 (0)	1 (1.3)	1 (1.0)
No. of prior MDEs, mean ± SD	2.9 ± 3.9	2.1 ± 2.3	2.2 ± 2.8
Vortioxetine dose (mg/day), mean ± SD^a	16.7 ± 3.7	18.1 ± 2.1	17.8 ± 2.6

MDE, major depressive episode; SD, standard deviation.
^aMean daily vortioxetine dose over the treatment period, calculated as the total dose received divided by the number of exposure days.

- Patients had severe symptoms of depression and anxiety at baseline, as well as significantly impaired overall functioning and HRQoL (Table 2)
- Vortioxetine dosage was increased to 20 mg/day in 94 patients after 1 week
- 87 patients were receiving vortioxetine 20 mg/day at week 4 and continued on this dose until study end

Table 2. Outcome Assessment Scores at Baseline and LS Mean Change After 8 Weeks of Vortioxetine Treatment in Patients With MDD Comorbid With GAD

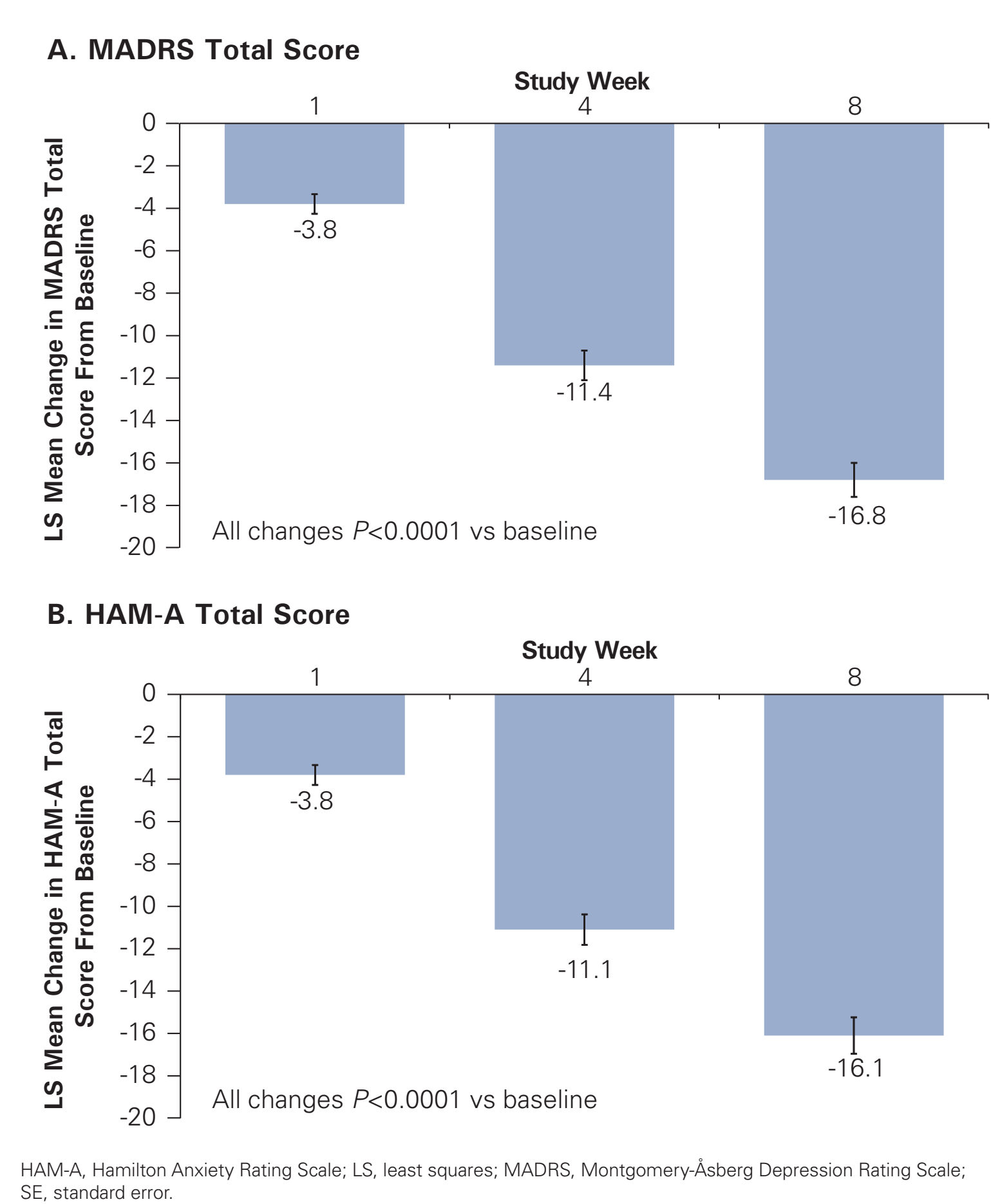
Outcome	Mean (SD) Score at Baseline (n=100)	LS Mean (SE) Change From Baseline at Week 8 ^a (n=96–98)
MADRS total score	29.5 (4.7)	−16.9 (0.80)
HAM-A total score	28.6 (4.9)	−16.1 (0.86)
HADS-D score	14.7 (4.3)	−8.2 (0.53)
HADS-A score	14.2 (3.4)	−7.2 (0.49)
CGI-S score	4.9 (0.6)	−2.1 (0.13)
FAST total score	42.1 (12.4)	−23.0 (1.6)
Q-LES-Q (LF) General Activities score (%)^b	38.5 (13.7)	25.7 (2.5)
Q-LES-Q (LF) Overall Satisfaction and Contentment score (%)^b	24.5 (18.6)	38.3 (3.4)

^aLS mean changes from baseline analyzed using a mixed model for repeated measurements; all changes, $P < 0.0001$ vs baseline.
^bn=99 at baseline. The Q-LES-Q (LF) numerical scale has been converted into a percentage scale by linear transformation of the scores into a scale of 0–100, where 0 corresponds to the worst score and 100 to the best score on the numerical scale.
 CGI-S, Clinical Global Impression-Severity; FAST, Functioning Assessment Short Test; GAD, generalized anxiety disorder; HADS-A, Hospital Anxiety and Depression Scale-Anxiety subscale; HADS-D, Hospital Anxiety and Depression Scale-Depression subscale; HAM-A, Hamilton Anxiety Rating Scale; LS, least squares; MADRS, Montgomery-Åsberg Depression Rating Scale; MDD, major depressive disorder; Q-LES-Q (LF), Quality of Life Enjoyment and Satisfaction Questionnaire (long form); SD, standard deviation; SE, standard error.

Effectiveness

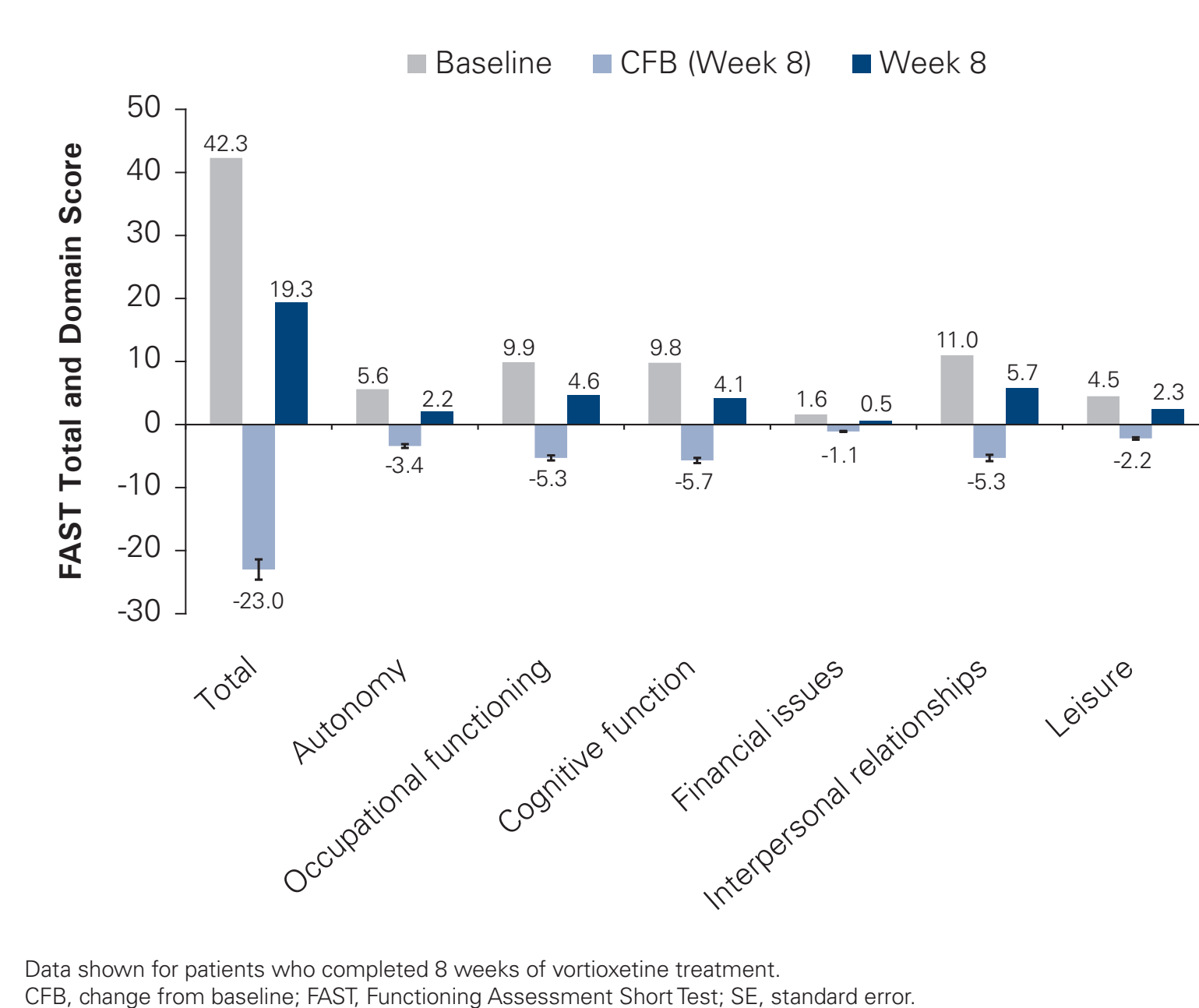
- After 8 weeks of vortioxetine treatment, statistically significant improvements from baseline were observed across all clinician- and patient-assessed symptoms of depression and anxiety, overall functioning, and HRQoL ($P < 0.0001$ for all scores shown vs baseline; Table 2)
- Statistically significant improvements in severity of depressive symptoms and anxiety were seen as early as week 1 (Figure 1)

Figure 1. LS Mean Change (SE) From Baseline in (A) MADRS Total Score and (B) HAM-A Total Score Over the 8 Weeks of Vortioxetine Treatment



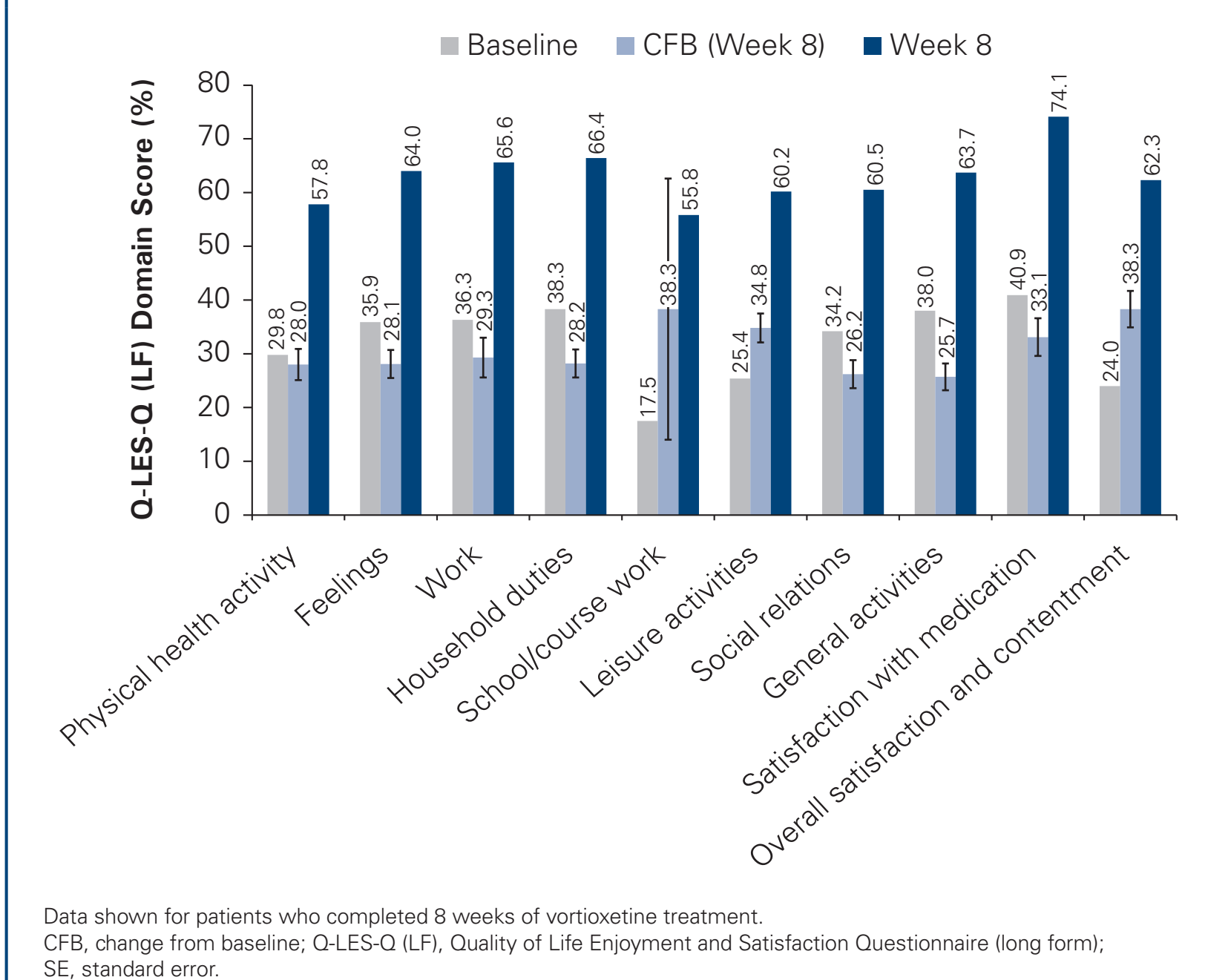
- Based on MADRS score at week 8, 60.8% of patients had achieved response and 35.1% were in remission
 - HAM-A response and remission rates were 54.6% and 42.3%, respectively
 - Overall, 50% of patients achieved response and 30% achieved remission on both scales
- Broad improvement was seen across all domains of functioning and HRQoL after 8 weeks of treatment with vortioxetine (Figures 2 and 3)

Figure 2. Mean FAST Total and Domain Scores at Baseline and Mean (SE) Change From Baseline After 8 Weeks of Vortioxetine Treatment



Data shown for patients who completed 8 weeks of vortioxetine treatment.
 CFB, change from baseline; FAST, Functioning Assessment Short Test; SE, standard error.

Figure 3. Mean Q-LES-Q (LF) Percentage Scores at Baseline and Mean (SE) Change From Baseline After 8 Weeks of Vortioxetine Treatment



Data shown for patients who completed 8 weeks of vortioxetine treatment.
 CFB, change from baseline; Q-LES-Q (LF), Quality of Life Enjoyment and Satisfaction Questionnaire (long form); SE, standard error.

- HAM-A and MADRS scores were significantly and strongly correlated with FAST total score (partial $r = 0.80$ and 0.76 , respectively; both $P < 0.0001$) and Q-LES-Q (LF) General Activities score (partial $r = -0.65$ and -0.62 , respectively; both $P < 0.0001$)

Tolerability

- Vortioxetine was well tolerated
 - There were no serious adverse events (AEs); only 2 patients withdrew from treatment primarily due to AEs
 - All AEs were of mild or moderate intensity; nausea was the most commonly reported AE (reported by 21% of patients)
 - No increases in AEs were reported in patients who increased vortioxetine dosage to 20 mg/day after the first week of treatment compared with patients who received 10 mg/day throughout the study

CONCLUSIONS

- This study provides evidence of the effectiveness and tolerability of higher therapeutic dosages of vortioxetine in patients with MDD comorbid with GAD who were either receiving vortioxetine as their first antidepressant treatment or switching to vortioxetine because of inadequate response to prior antidepressant therapy
- In this population of patients with severe MDD and severe GAD, vortioxetine demonstrated effectiveness in significantly reducing symptoms of both depression and anxiety. The beneficial effects were already significant after 1 week and continued to increase over the 8 weeks of treatment
- The marked improvement in symptoms of depression and anxiety was significantly correlated with broad improvements in overall functioning and HRQoL
- Findings support increasing vortioxetine dosage to 20 mg/day early in the course of treatment to achieve optimal therapeutic benefit in patients with MDD and comorbid GAD, and show that this may be achieved without compromising tolerability

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DISCLOSURES

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