Vortioxetine in Routine Clinical Practice: Results From the Real-Life Effectiveness of Vortioxetine (RELIEVE) Study

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INTRODUCTION

- Major depressive disorder (MDD) affects more than 264 million people worldwide and is associated with a negative impact on individuals' mental and physical health[1,2]
- MDD is also associated with significant psychosocial functioning and cognitive impairments[3]
- Marked functional impairment, as assessed using the Sheehan Disability Scale (SDS), can continue after initiating antidepressant therapy for patients with MDD[4,5]
- An overall improvement in patient functioning has previously been observed in randomized clinical trials of patients with MDD administered vortioxetine,[6,7] a multimodal antidepressant that has been authorized for use since 2013 in the US and is now approved in more than 80 countries worldwide[8]

OBJECTIVE

- To evaluate the real-world effectiveness of vortioxetine in routine clinical practice on overall functioning, cognitive functioning, depressive symptom relief, and health-related quality of life (QoL) in patients with MDD

METHODS

Study Design

- RELIEVE was a global, prospective, single-arm, observational cohort study (ClinicalTrials.gov identifier NCT03555136) of patients with MDD treated with vortioxetine
- Patients were followed for 24 weeks, with 3 visits planned at baseline, week 12 (±4 weeks), and week 24 (±4 weeks)
  - At each visit, outcomes assessments were conducted to evaluate the effectiveness of treatment with vortioxetine

Eligibility Criteria

- Eligible patients were aged 18 years or older and initiating outpatient vortioxetine treatment for diagnosis of a major depressive episode (MDE) (according to local diagnostic criteria); vortioxetine was prescribed by a general practitioner or psychiatrist (according to local prescribing regulations)
- Patients were excluded from the study if they:
  - Had schizophrenia, bipolar disorder, substance use disorder, or neurodegenerative diseases significantly impacting their cognitive functioning
  - Were considered at significant risk of suicide or attempted suicide within the last 6 months

Endpoints

- The primary endpoint was mean change in functioning from baseline to weeks 12 and 24, as measured by the SDS, a validated tool for assessing functional impairment in patients with MDD
- Secondary endpoints evaluated changes from baseline in:
  - Cognitive symptoms: Digit Symbol Substitution Test (DSST) and Perceived Deficits Questionnaire – Depression – Five items (PDQ-D-5)
  - Functioning domains: SDS subscores
  - Sexual function: Arizona Sexual Experience Scale (ASEX)
  - Depression severity: Patient Health Questionnaire – Nine items (PHQ-9), Clinical Global Impression Scale – Severity (CGI-S), and CGI – Improvement (CGI-I)
  - QoL: EuroQoL Five Dimensions Five Levels (EQ-5D-5L)

Statistical Analysis

- Effectiveness analyses were performed on the full analysis set (FAS) for both the primary and secondary endpoints
  - All endpoints were analyzed using a linear mixed model for repeated measure with visit as the fixed effect
  - The mixed model was adjusted for clinically relevant covariates (ie, age, sex, education level, duration of MDE at baseline, baseline comorbidities, and baseline depression severity)

RESULTS

Patient Disposition

- A total of 994 patients were recruited from across 103 sites in Canada, France, Italy, and the US
  - The safety population included 985 patients who provided informed consent and initiated vortioxetine therapy
  - The FAS included 737 patients who met the eligibility criteria, initiated vortioxetine, and attended ≥1 post-baseline visit

Baseline Characteristics

- Most patients were White/Caucasian females, with a mean age of ~49 years (**Table 1**)
  - Most patients (56%) resided in Europe and approximately half had a tertiary education
- On average, patients had 4.4 previous MDEs, and the mean duration of the current MDE at baseline was approximately 47 weeks
  - For most patients, vortioxetine was used as a second-line or later-line treatment (56.5%), and the starting dose was ≤10 mg (82.6%)
- Approximately three-quarters of patients had at least one comorbidity
  - More than half of the patients had comorbid anxiety

Table 1. Baseline Characteristics and Demographics of Patients in the RELIEVE Study

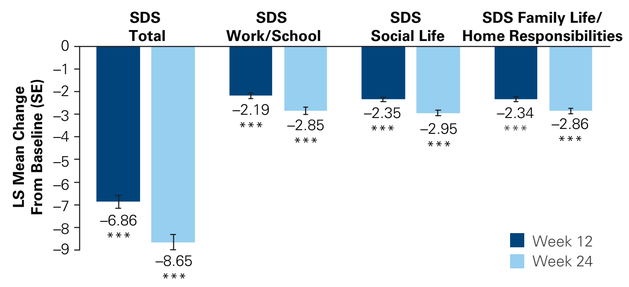
Characteristics	N=737
Sex, female, n (%)	473 (64.2)
Age, years, mean (SD)	49.3 (15.4)
>65 years, n (%)	115 (15.6%)
Race/ethnicity, n (%)	
White/Caucasian	597 (81.0)
Hispanic/Latino	13 (1.8)
Black/African American	21 (2.8)
Asian	6 (0.8)
Unspecified	100 (13.6)
BMI[a], kg/m², mean (SD)	27.5 (6.0)
Overweight/obese (≥25.0, n(%)	448 (61.7)
Country, n (%)	
Canada	76 (10.3)
France	184 (25.0)
Italy	231 (31.3)
US	246 (33.4)
Patients with at least one comorbidity, n (%)*	543 (73.7)
Comorbid anxiety, n (%)	413 (56)
Occupation, n %	
Working	411 (55.8)
Non-working	326 (44.2)
MDD history[b], mean (SD)	
Mean number of previous MDEs	4.4 (9.1)
Mean duration of current MDE at baseline, weeks	47.0 (140.8)
Time (years) since MDD diagnosis, mean (SD)	11.2 (12.1)
Vortioxetine treatment line, n (%)	
First	321 (43.6)
Second	257 (34.9)
Third+	159 (21.6)
Outcome assessments at baseline, mean (SD)	
SDS total score[c]	19.6 (6.6)
ASEX[d]	22.0 (6.5)
PHQ-9	16.5 (5.5)
PDQ-D-5	11.2 (4.9)
DSST[b]	42.6 (16.8)
EQ-5D-5L[c]	0.7 (0.2)
CGI-S	4.3 (0.9)

[a]n=726; [b]n=735; [c]n=736; [d]n=701; [e]n=695.
*Patients present various comorbidities at study initiation, including sleep disorders (22%), cardiovascular disease (16.7%), chronic pain (8.5%), diabetes (7.2%), chronic fatigue (6.1%), neurological disorder (6.0%), smoking (4.7%).
ASEX, Arizona Sexual Experience Scale; BMI, body mass index; CGI-S, Clinical Global Impression Scale – Severity; DSST, Digit Symbol Substitution Test; EQ-5D-5L, EuroQoL Five Dimensions Five Levels; MDD, major depressive disorder; MDE, major depressive episode; PDQ-D-5, Perceived Deficits Questionnaire – Depression – Five items; PHQ-9, Patient Health Questionnaire – Nine items; SD, standard deviation; US, United States.

Clinical Outcomes Following Vortioxetine Treatment in a Real-World Setting

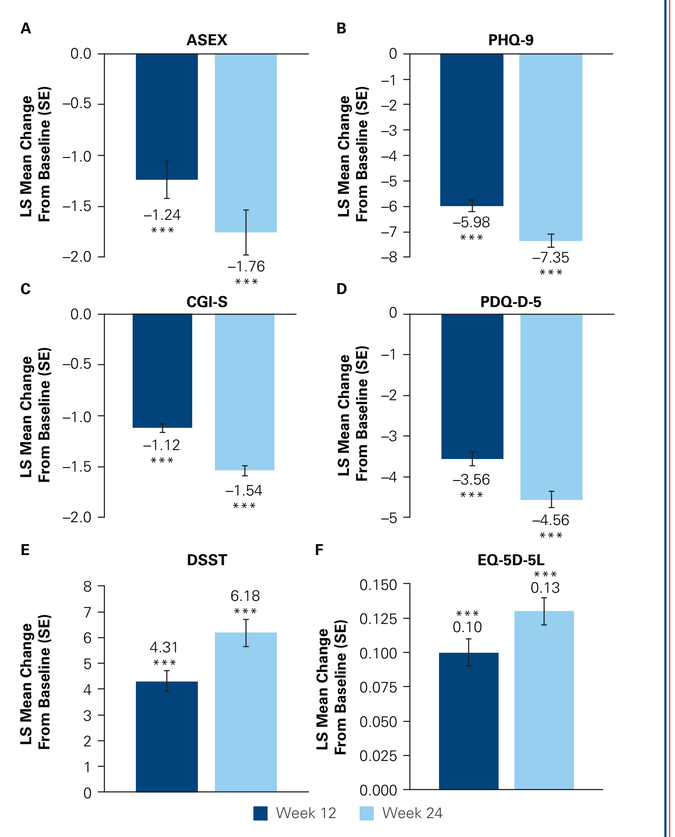
- SDS total score was significantly reduced from 19.62 (95% confidence interval [CI], 19.15–20.08) at baseline to 12.75 (95% CI, 12.14–13.36) and 10.96 (95% CI, 10.32–11.61) at weeks 12 and 24, respectively (**Figure 1**)
  - Significant improvements were also observed for all SDS subscores (**Figure 1**)
- Improvements in cognitive function (DSST and PDQ-D-5), sexual function (ASEX), depression severity (PHQ-9 and CGI-S), and QoL (EQ-5D-5L) were also observed at weeks 12 and 24 (**Figure 2**)

Figure 1. Changes in Adjusted LS Mean Scores From Baseline to Weeks 12 and 24 for SDS Total Score and SDS Subscores



*** *P* <0.001 vs. baseline. LS, least squares; SDS, Sheehan Disability Scale; SE, standard error. At baseline, SDS work/school subscore (SD) was 6.31 (2.69); social life subscore (SD) was 6.68 (2.41); and family life subscore (SD) was 6.56 (2.40).

Figure 2. Changes in Adjusted LS Mean Scores From Baseline to Weeks 12 and 24 for Sexual Dysfunction (A), Depression Severity (B,C), Cognitive Symptoms (D,E), and QoL (F)

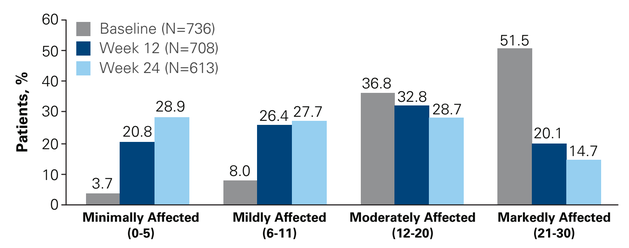


*** *P* <0.001 vs. baseline. ASEX, Arizona Sexual Experience Scale; CGI-S, Clinical Global Impression Scale – Severity; DSST, Digit Symbol Substitution Test; EQ-5D-5L, EuroQoL Five Dimensions Five Levels; LS, least squares; PDQ-D-5, Perceived Deficits Questionnaire – Depression – Five items; PHQ-9, Patient Health Questionnaire – Nine items; QoL, quality of life; SE, standard error.

Shift in SDS Categories Following Vortioxetine Treatment

- The proportion of patients with severe functional impairment (SDS total score >20) decreased from 51.5% at baseline to 20.1% at week 12 and further decreased to 14.7% at week 24 (**Figure 3**)
- After 24 weeks of vortioxetine treatment, the majority (56.6%) of patients reported mild or minimal functional impairment compared with only 11.7% of patients at baseline (**Figure 3**)
  - A similar trend was also reflected in all SDS subscores

Figure 3. SDS Total Score Category at Baseline and Weeks 12 and 24

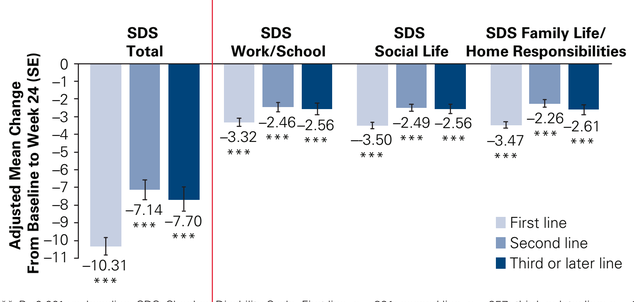


SDS, Sheehan Disability Scale.

Improvement From Baseline to Week 24 Per Vortioxetine Line of Treatment

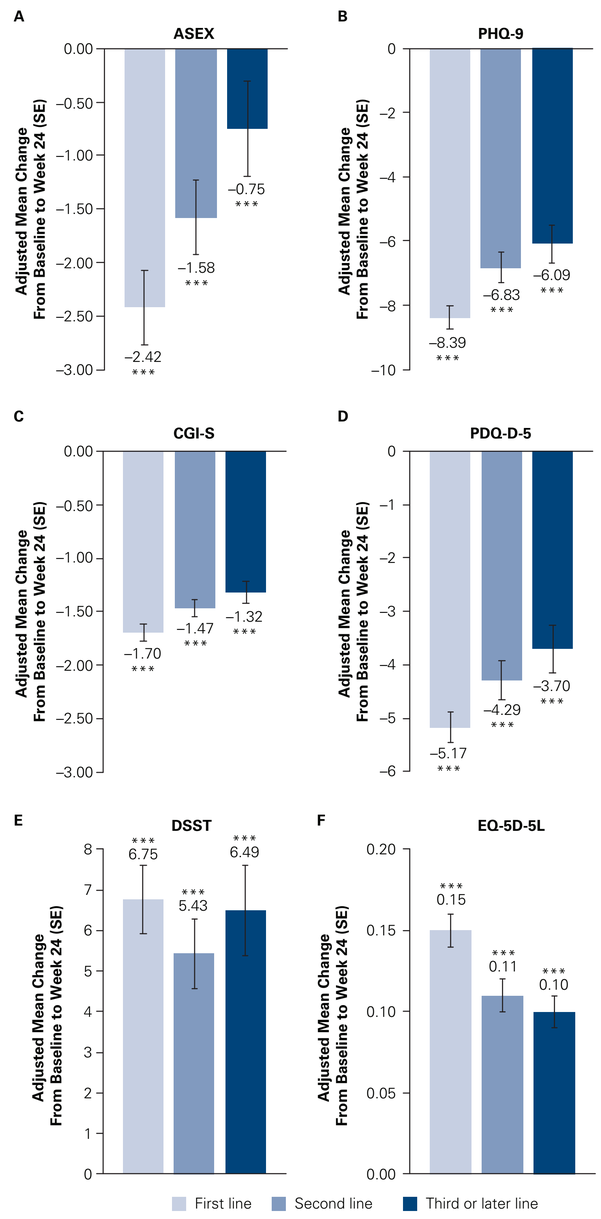
- Of 737 patients included in the FAS, vortioxetine was administered as the first, second, and third or later line of treatment to 321, 257, and 159 patients, respectively
- SDS total score and subscores significantly decreased from baseline to week 24 in patients regardless of vortioxetine treatment line (**Figure 4**)
  - Significant improvements were also observed for all secondary endpoints, regardless of treatment line, with the exception of ASEX scores where a numerical reduction (not statistically significant) was observed for third-line or later-line vortioxetine treatment (**Figure 5**)

Figure 4. Adjusted Mean Change From Baseline to Week 24 Per Line of Treatment for SDS Total Score and SDS Subscores



*** *P* <0.001 vs. baseline. SDS, Sheehan Disability Scale. First-line, n = 321; second-line, n = 257; third- or later-line; n = 159; SE, standard error.

Figure 5. Adjusted Mean Change From Baseline to Week 24 Per Line of Treatment for Sexual Function (A), Depression Severity (B,C), Cognitive Symptoms (D,E), and QoL (F)



*** p <0.001 vs. baseline. First-line, n = 321; second-line, n = 257; third- or later-line; n = 159. ASEX, Arizona Sexual Experience Scale; CGI-S, Clinical Global Impression Scale – Severity; DSST, Digit Symbol Substitution Test; EQ-5D-5L, EuroQoL Five Dimensions Five Levels; PDQ-D-5, Perceived Deficits Questionnaire – Depression – Five items; PHQ-9, Patient Health Questionnaire – Nine items; QoL, quality of life; SE, standard error.

Safety Analysis

- In total, 21.2% of patients reported an adverse event during the 24 weeks of vortioxetine treatment (**Table 2**)
- No new safety concerns were reported

Table 2. Summary of the Most Common AEs (>1%)

	N=985
Any AE, n (%)	209 (21.2)
Most common AEs, or AEs occurring in >1% of patients, n (%)	
Nausea	81 (8.2)
Headache	15 (1.5)
Pruritus	15 (1.5)
Anxiety	14 (1.4)

AE, adverse event.

CONCLUSIONS

- Results of this real-world study demonstrate the long-term effectiveness and tolerability of vortioxetine for the treatment of MDD in a large and heterogeneous patient population representative of that encountered in routine clinical practice settings
- The effectiveness of vortioxetine was observed in terms of improved functioning, decreased depression severity, improved cognitive and sexual function, and improved QoL
- Patients may benefit from early initiation of vortioxetine, as shown across various measures, compared to its use as a second or third line treatment in a current MDE
- Vortioxetine was generally well tolerated
  - The safety findings were consistent with the established tolerability profile of vortioxetine
- These data support vortioxetine as an effective and beneficial option for treatment of patients with MDD in routine clinical practice

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DISCLOSURES

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