Personalized Goal Attainment After a Switch to Vortioxetine in Adults With Major Depressive Disorder (MDD): Results of a Phase 4, Open-Label Clinical Trial

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BACKGROUND

- Response to treatment of major depressive disorder (MDD) is generally evaluated by using traditional, validated clinician- and patient-reported outcome measures.[1,2]
- Traditional standard rating scales may miss meaningful changes specific to each patient's condition.[2] A scale that incorporates patient expectations from treatment in an individualized manner may be beneficial to patients and clinicians to achieve a fuller picture of a patient's response to treatment.[2]
- The Goal Attainment Scale (GAS) utilizes an individualized goal development approach; it has been used in clinical care and program assessment for other medical and non-medical indications.[3]
- This study evaluated goal achievement using the GAS adapted for depression (GAS-D) in patients with MDD after a switch to vortioxetine from a previous antidepressant medication.
- To our knowledge, this is the first study to adapt the GAS as a primary outcome measure for MDD.

OBJECTIVES

Primary Objective

- Evaluate the effectiveness of a 12-week course of treatment with vortioxetine (10-20 mg) on goal achievement, as measured by the GAS-D score, in patients with MDD requiring a switch in antidepressant treatment.

Additional Objectives

- Evaluate the effectiveness of treatment with vortioxetine on depressive symptoms, clinical global impression, cognitive functioning, and well-being in patients with MDD.
- Determine treatment response and remission rates, as well as evaluate the safety and tolerability of vortioxetine.

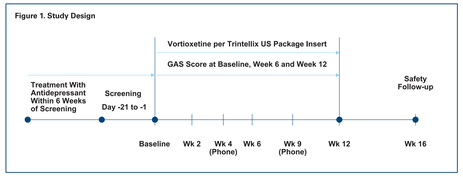
There are three separate presentations of results from this clinical study at this Congress. This poster focuses on goal achievement and change in patient and clinician ratings of depression severity, cognitive functioning and performance, and well-being. Functional outcomes and healthcare utilization are presented in Poster **#231**[4] at this Congress, and the validity of the GAS-D is presented in Poster **#203**.[5]

METHODS

Study Design

- Phase 4, open-label, multicenter clinical trial in the United States (ClinicalTrials.gov ID NCT02972632) evaluating the real-world effectiveness of a 12-week course of vortioxetine treatment on goal achievement. The study schema is shown in **Figure 1**.

Figure 1. Study Design



Key Eligibility Criteria

- Adults (ages 18 to 65, inclusive) with MDD
- Recent (within 6 weeks of screening) or current treatment with an approved antidepressant for at least 6 weeks
- Considered appropriate for a change in antidepressant medication based on investigator judgment in collaboration with the patient
- Scores on Patient Health Questionnaire (PHQ-9) ≥5 and Clinical Global Impression Severity of Illness (CGI-S) ≥4 at screening

Key Exclusion Criteria

- Current psychiatric disorders other than MDD (except nonprimary concurrent anxiety), other illness or condition that may compromise the study in the opinion of the investigator
- Considered to be at imminent risk for hospitalization due to severe depression in the opinion of the investigator. Recent hospitalization due to MDD within 3 months prior to screening
- Significant risk of suicide or has made an actual suicide attempt in the previous 6 months prior to screening

Procedures

- All patients were initiated on vortioxetine 10 mg, and based on the discretion of the clinical investigator, were titrated to 20 mg.
  - Tapering from 10 mg to 5 mg was allowed based on the patient's response and tolerability, as judged by the investigator.
- Treatment goals were jointly determined by patients and clinicians using the GAS-D approach (**Figure 2**).
- Each patient and their clinician worked to establish three goals at baseline:
  - One goal was determined based on the patient's self-defined objectives.
  - Two goals were selected from the predefined domains representing MDD residual symptoms, antidepressant side effects, and common reasons for a change in antidepressant medication.

Figure 2. The Goal-Setting and Domain-Defined Approach

Domain				
Psychological	Motivation	Emotional	Physical/Function	Cognition
Sub-domain*				
• Depressed • Anxious • Sad • Irritable	• Lack of motivation • Decreased social interaction	• Low self-esteem • Lack of enjoyment/pleasure • Feelings of guilt • Feeling inappropriate or that one doesn't fit in • Feeling isolated • Lack of interest	• Fatigue • Insomnia • Muscle tension • Decreased sex drive • Weight gain • Decreased appetite • Weight loss • Sleeping too much • Talking or moving slowly • GI disturbances	• Problems concentrating • Short-term memory problems • Difficulty staying focused • Difficulty paying attention • Problems thinking clearly • Difficulty multitasking • Brain is "cloudy" • Losing your train of thought

*Not a comprehensive list; can also include tolerability concerns
GI, gastrointestinal

- In the GAS-D approach, each goal is assigned to a level of -2, -1, 0, 1, or 2 (**Figure 3**). Level 0 represents the target outcome for the patient/clinician to consider the goal as having been achieved.

Figure 3. Scoring the Goal Attainment Scale (GAS)

- Collaborative goal-setting exercise as a means of tracking individual progress over time
- Goals must be meaningful to the patient
- Good goals are characterized by being specific, measurable, achievable, realistic, and time-bound
- Progress is measured against equidistant benchmarks ranging from -2 to +2

- Sample goals (as examples provided to patients at baseline) are listed in **Table 1**

Table 1. Sample Goals at Baseline

Type of Goal by Sub-domain Category	Example of Goals
Lack of enjoyment/pleasure	Spend fun time with family (offer to play games) three times per week.
Fatigue	Make time to care for myself (walk around the park with my grandson for at least 15 minutes, brief exercise (leg lifts or brief walks)) three times per week.
Decreased social interaction	Increase social interaction: call grandkids two times per week plus two short outings (2 hours) a week.
Lack of interest	Work on hobbies such as painting, refinishing furniture, and writing for 3 hours a week

GAS-D Score Calculation

- The GAS-D score was based on standardization to a central value of 50.
- Formula to compute the GAS score:

$$\text{GAS Score} = 50 + \frac{10 \times \sum(w_i x_i)}{\sqrt{(0.7 \times \sum w_i^2) + 0.3 \times (\sum w_i)^2}}$$

  - Calculation and interpretation of GAS scores includes several potential methods, including weighted averages, which were used in this study.

Outcome Measures

- The primary outcome measure was the proportion of patients who achieved their pre-identified goals as demonstrated by a GAS-D score of ≥50 at week 12.
  - Change from baseline in mean GAS-D score at weeks 6 and 12 were also assessed.
- Additional outcomes included change from baseline at 6 and/or 12 weeks on the following:
  - Patient Health Questionnaire-Depressive Symptoms (PHQ-9) – patient-reported symptoms
  - Perceived Deficits Questionnaire-Depression (PDQ-D) – patient-reporting cognitive functioning
  - Digit Symbol Substitution Test (DSST) – cognitive performance, administered by study staff
  - World Health Organization Well-Being Index (WHO-5) – patient-reported emotional well-being
  - Clinical Global Impression Scale-Severity (CGI-S) – clinician's global impression of illness severity
  - Clinical Global Impression Scale-Improvement (CGI-I) – clinician's impression of improvement
  - Virtual Reality Functional Capacity Assessment Tool (VRFCAT) – functional capacity
- Safety evaluations were adverse events (AEs); AEs leading to discontinuation; changes in weight; Columbia-Suicide Severity Rating Scale (C-SSRS).

Statistical Analyses

- Statistical analysis was performed using SAS version 9.4.
- The estimated proportion and 95% confidence interval (CI) were calculated for the primary endpoint.
- Paired *t* tests were performed for change from baseline along with *P* values for efficacy variables.
- $P<0.05$ was considered to be statistically significant.

RESULTS

Patient Characteristics (Table 2)

- 123 patients were enrolled; 86% (n=106) completed treatment
- Mean age was 45 years; 83% were women and 69% were white
- 67 patients (57.7%) were educated to college level or higher
- Mean PHQ-9 score (at baseline) was 15.7, indicating moderately severe depression
- A majority (62%) of patients switched to vortioxetine due to "inadequate response" or because their previous antidepressant was "not working as expected."

Table 2. Baseline Characteristics

Characteristics (N=122)	
Sex	
Male, n (%)	21 (17.2)
Female, n (%)	101 (82.8)
Age, mean years (SD)	45.3 (12.2)
Age ≤55 years, n (%)	95 (77.9)
Race, n (%)	
White	83 (69.2)
Black or African American	28 (23.3)
Asian	5 (4.2)
Native Hawaiian or Other Pacific Islander	1 (0.8)
Multiracial[a]	3 (2.5)
Unknown	2
Ethnicity, n (%)	
Hispanic or Latino	28 (23.0)
Employment status, n (%)[b]	
Employed full-time	32 (27.6)
Employed part-time	22 (19.0)
Self-employed	15 (12.9)
Not employed[c]	48 (41.7)
BMI, mean kg/m² (SD)	34.1 (9.7)
PHQ-9[d], mean (SD)	15.7 (4.8)

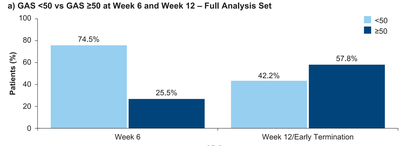
[a] 13 (10.6) patients withdrew from the study: 10 voluntarily withdrew, 4 lost to follow-up, 2 discontinued following an adverse event.
[b]Patients could select more than one race option on the case report form; %=/115. In cases of multiple employment statuses per patient, the patient is counted as many times as the number of employment statuses. Percentages are based on the number of patients in the full analysis set. Data for one patient was missing. [c]Includes unemployed, student, retired, non-working spouse, and other; %=/110.
BMI, body mass index; PHQ-9, Patient Health Questionnaire-Depressive Symptoms; SD, standard deviation.

GAS-D Scores

- For the primary outcome measure, 57.8% of patients who completed week 12 achieved a GAS-D score of ≥50 (indicating successful goal attainment) with significant changes from baseline ($P<0.001$) (**Figure 4a** and **4b**).

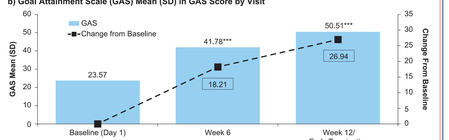
Figure 4. GAS-D Scores

a) GAS <50 vs GAS ≥50 at Week 6 and Week 12 – Full Analysis Set



CI (0.485, 0.671);
Total n=108 (week 12).

b) Goal Attainment Scale (GAS) Mean (SD) in GAS Score by Visit



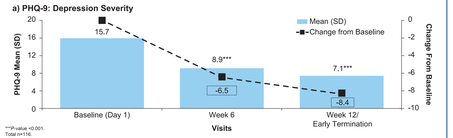
***P-value <0.001.
Total n=116.
Standard deviation at baseline=0.07, at 6 weeks=11.46, at 12 weeks=13.58.

Additional Outcome Measures

- Measures of depression severity, cognitive function, cognitive performance, emotional well-being, and clinician's global impression of illness severity all showed statistically significant improvements from baseline at 6 and 12 weeks (**Figure 5 a-e**).

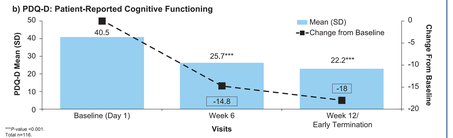
Figure 5. Change From Baseline on Standard Measures

a) PHQ-9: Depression Severity



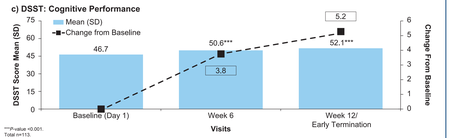
***P-value <0.001.
Total n=116.
Standard deviation at baseline=4.79; at 6 weeks=5.87; at 12 weeks=5.58.

b) PDQ-D: Patient-Reported Cognitive Functioning



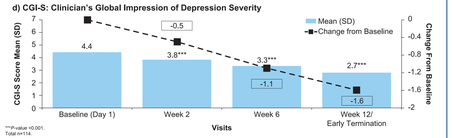
***P-value <0.001.
Total n=116.
Standard deviation at baseline=14.87; at 6 weeks=14.92; at 12 weeks=15.96.

c) DSST: Cognitive Performance



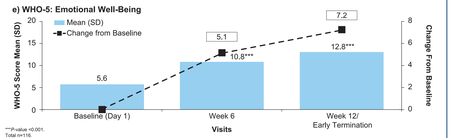
***P-value <0.001.
Total n=113.
Standard deviation at baseline=11.06; at 6 weeks=12.91; at 12 weeks=11.66.

d) CGI-S: Clinician's Global Impression of Depression Severity



***P-value <0.001.
Total n=114.
Standard deviation at baseline=0.50; at 2 weeks=0.76; at 6 weeks=0.99; at 12 weeks=1.05.

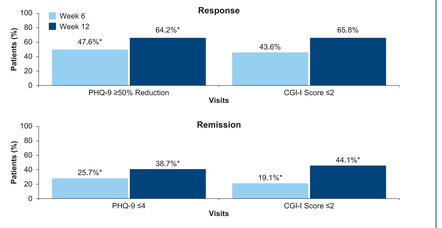
e) WHO-5: Emotional Well-Being



***P-value <0.001.
Total n=116.
Standard deviation at baseline=3.49; at 6 weeks=5.49; at 12 weeks=6.15.

- Treatment response (≥50% total score reduction on PHQ-9 and CGI-I ≤2) was reported by 64.2% of patients and remission (PHQ-9 ≤4 and CGI-I ≤2) by 38.7% at week 12 (**Figure 6**).

Figure 6. Response and Remission Rates During Vortioxetine Treatment



*P-value <0.0001.

Safety

- The safety profile of vortioxetine during this study was consistent with the vortioxetine prescribing information (**Table 3**).
- 117 adverse events were reported by 59 patients.
  - Adverse events were most commonly gastrointestinal (34%), nervous system (21%), or psychiatric (20%) disorders and were generally mild or moderate in severity.
- Seven adverse events (in six patients) led to discontinuation of study treatment.
  - Four cases of psychiatric disorders, and one case each of headache, nausea, and vomiting.
- Two serious treatment-emergent adverse events (depression and suicidal ideation) were reported in one patient, leading to treatment discontinuation.
  - These events were determined to be not related to the study drug.
- No suicides or deaths occurred during the study.

Table 3. Adverse Events Reported by ≥5% of Patients

Adverse event (N=122)	n (%)
Patients with any treatment-emergent adverse event	63 (68.0)
Nausea	26 (21.3)
Headache	11 (9.0)
Anxiety	8 (6.6)
Constipation	7 (5.7)
Diarrhea	7 (5.7)

CONCLUSIONS

- This study showed positive results on the primary outcome, with a majority of patients treated with vortioxetine reaching their personalized treatment goals after 12 weeks.
- In patients with MDD requiring an antidepressant switch due to inadequate efficacy, vortioxetine was effective in helping them reach personalized and meaningful treatment goals.
- Significant improvements were also realized in many other areas, including overall depressive symptoms, cognitive function, cognitive performance, emotional well-being, and clinician-rated improvement—all key indicators of progress toward functional recovery.
- Vortioxetine was safe and well tolerated in this real-world setting; the safety profile was consistent with product labelling.
- Results for the GAS-D primary endpoint were supported by improvements on several standard patient and clinician-reported measures, demonstrating that improvement on personalized goals is an appropriate method of evaluating overall improvement in MDD.
- The findings support using this novel, patient-centric approach to assessing outcomes of MDD treatment.
- The GAS-D is a shared decision-making approach to help clinicians understand what matters most to the patient during treatment for MDD by using individualized treatment goals. This patient-centered approach offers a unique way to assess response to treatment and progress towards functional recovery.

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DISCLOSURES

Maggie McCue, Sara Sarkey, are employees of Takeda Pharmaceuticals U.S.A., Inc. Lisa Mucha was an employee of Takeda Pharmaceuticals U.S.A., Inc., at the time of this study. Anna Eramo is an employee of Lundbeck LLC. Clement François was an employee of Lundbeck LLC at the time of this study. Sagar V. Parikh is a consultant to Takeda and Sunovion, has a research contract with Assurex Health, and owns shares in Mensante Corporation.

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