Real-Life Effectiveness of Vortioxetine on Goal Achievement and Work Productivity in Japanese Patients With Major Depressive Disorder: The VGOAL-J Study

Koichiro Watanabe,[1] Tomiki Sumiyoshi,[2] Masaki Kato,[3] Toshiaki Kikuchi,[4] Yoshiya Moriguchi,[5] Daniel Oudin Åström,[6] Michael Cronquist Christensen[6]

[1]Department of Neuropsychiatry, Kyorin University School of Medicine, Tokyo, Japan; [2]Department of Preventive Intervention for Psychiatric Disorders, National Institute of Mental Health, National Center of Neurology and Psychiatry, Tokyo, Japan; [3]Department of Neuropsychiatry, Kansai Medical University, Osaka, Japan; [4]Keio University School of Medicine, Department of Neuropsychiatry, Tokyo, Japan; [5]Lundbeck Japan K.K., Tokyo, Japan; [6]H. Lundbeck A/S, Valby, Denmark

BACKGROUND

- Major depressive disorder (MDD) is the leading cause of disability worldwide[1,2] and has been reported to reduce productivity in the workplace,[3] an essential component of functionality for patients. In Japan, a higher prevalence of depression was reported among the employed population compared with other countries[4]
- In addition to the assessment of conventional outcomes, measures of personal recovery customized for each individual with MDD have been drawing attention in relation to therapeutic response. Accordingly, the Goal Attainment Scale adapted for depression (GAS-D) has been developed[1]
- Also importantly, workplace productivity is adversely affected by cognitive impairment associated with depression[4]
- Vortioxetine, a multimodal antidepressant, has demonstrated efficacy in randomized clinical trials in patients with MDD.[5-7] However, little information has been available in Japan on the effectiveness of vortioxetine for goal attainment and work productivity in patients among the working population

OBJECTIVES

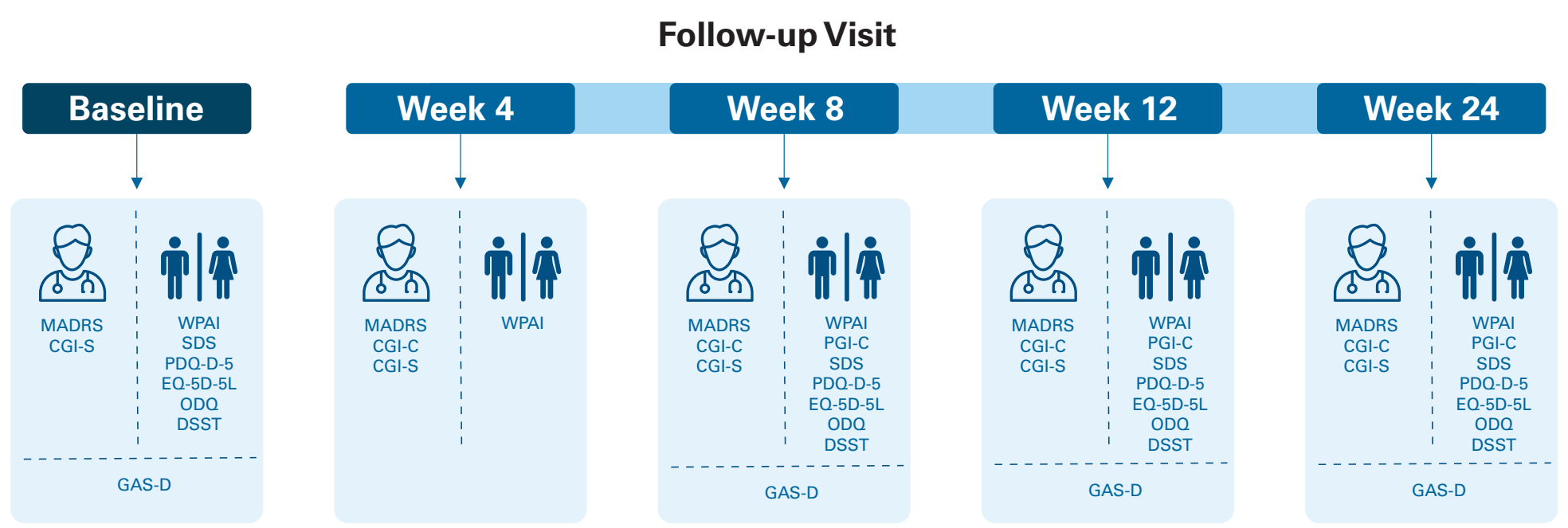
- To assess the effectiveness of treatment initiated with vortioxetine on goal achievement and work productivity in employed patients with MDD in the clinical practice setting

METHODS

Study Design

- VGOAL-J is an observational, multisite, single-arm, prospective cohort study conducted in Japan, targeting employed patients with MDD treated with vortioxetine in an outpatient setting
- Patients were followed-up for 6 months with visits planned at baseline and weeks 4, 8, 12, and 24
  - At each visit, outcome assessments were conducted to evaluate the effectiveness of treatment initiated with vortioxetine (**Figure 1**)

Figure 1. Outcome Assessments Timeline



CGI-C, Clinical Global Impressions–Change; CGI-S, Clinical Global Impressions–Severity; DSST, Digit Symbol Substitution Test; EQ-5D-5L, EuroQol Five Dimensions Five Levels; GAS-D, Goal Attainment Scale for Depression; MADRS, Montgomery-Åsberg Depression Rating Scale; ODQ, Oxford Depression Questionnaire; PDQ-D-5, Perceived Deficits Questionnaire–Depression 5-item; PGI-C, Patient Global Impression of Change; SDS, Sheehan Disability Scale; WPAI, Work Productivity and Activity Impairment questionnaire.

Eligibility Criteria

- Eligible patients were outpatients, aged 20 to 65 years, diagnosed with a major depressive episode (MDE), and currently employed. Treatment with vortioxetine was initiated (according to the local Japanese label) by general or psychiatric practitioners
- Data were excluded from the study if the patient was:
  - Prescribed >1 antidepressant on the day of the baseline visit
  - Expected not to return to work within 6 months according to the investigator's opinion
  - Diagnosed with schizophrenia, bipolar disorder, substance use disorder, or a neurodegenerative disease significantly impacting their cognitive functioning
  - Considered at significant risk of suicide or attempted suicide within the last 6 months
  - Pregnant, ≤6 months postpartum, or breastfeeding

Endpoints

Primary Endpoints

- To assess the effectiveness of treatment initiated with vortioxetine on goal achievement, captured by proportion of patients who achieved the preset goals overall on the GAS-D at week 12
- To evaluate changes in work productivity over 24 weeks, as measured by the Work Productivity and Activity Impairment questionnaire (WPAI)
  - WPAI contains 4 metrics: absenteeism (missed time at work), presenteeism (reduced productivity while at work), work productivity loss, and activity impairment; each uses a different response scale, with higher scores indicating greater impairment

Key Secondary Endpoints

- To assess the effectiveness of treatment initiated with vortioxetine on overall functioning and depressive, cognitive, and emotional symptoms (**Figure 1**)
  - Physician-rated assessments:
    - Patient goal achievement at weeks 8 and 24: GAS-D
    - Depressive symptoms: Montgomery-Åsberg Depression Rating Scale (MADRS), Clinical Global Impressions–Severity (CGI-S), and CGI–Change (CGI-C)
  - Patient-reported outcomes:
    - Overall functioning and functioning domains: Sheehan Disability Scale (SDS)
    - Emotional symptoms: Oxford Depression Questionnaire (ODQ)
    - Cognitive symptoms and performance: Perceived Deficits Questionnaire–Depression 5-item (PDQ-D-5) and Digit Symbol Substitution Test (DSST)
    - Health status and quality of life (QoL): EuroQol Five Dimensions Five Levels (EQ-5D-5L), EuroQol Visual Analog Scale (EQ-VAS), and Patient Global Impression of Change (PGI-C)

Safety Assessment

- Adverse events (AEs) and serious AEs (SAEs) were assessed throughout the study

GAS-D Satisfaction Survey

- Patient and clinician perceptions of the GAS-D approach were captured with survey responses

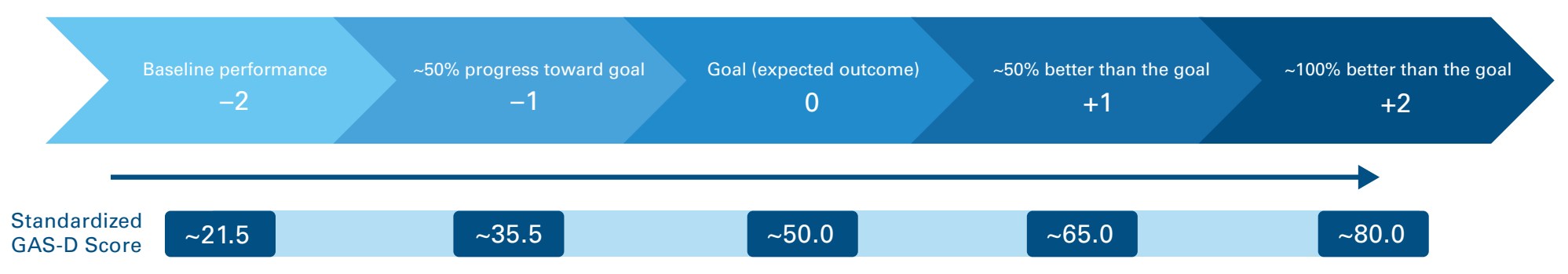
GAS-D Rating and Scoring

Two customized treatment goals determined by the patient and clinician were assessed at baseline and evaluated on a 5-point rating scale (–2 to +2) at each visit, where –2 indicated baseline status and +2 indicates progress 100% better than goal (**Figure 2**)

- Composite GAS-D scores were then transformed to a standardized score where scores ≥50 indicated all goals achieved or exceeded overall and <50 indicated goals achieved less than expected overall[1]
- Overall "goal achievement" was defined as a GAS-D score ≥50

Scan here for further details of the GAS-D (including the calculation method of the standardized GAS-D score from the 5-point ratings)

Figure 2. GAS-D rating and scoring



Statistical Analysis

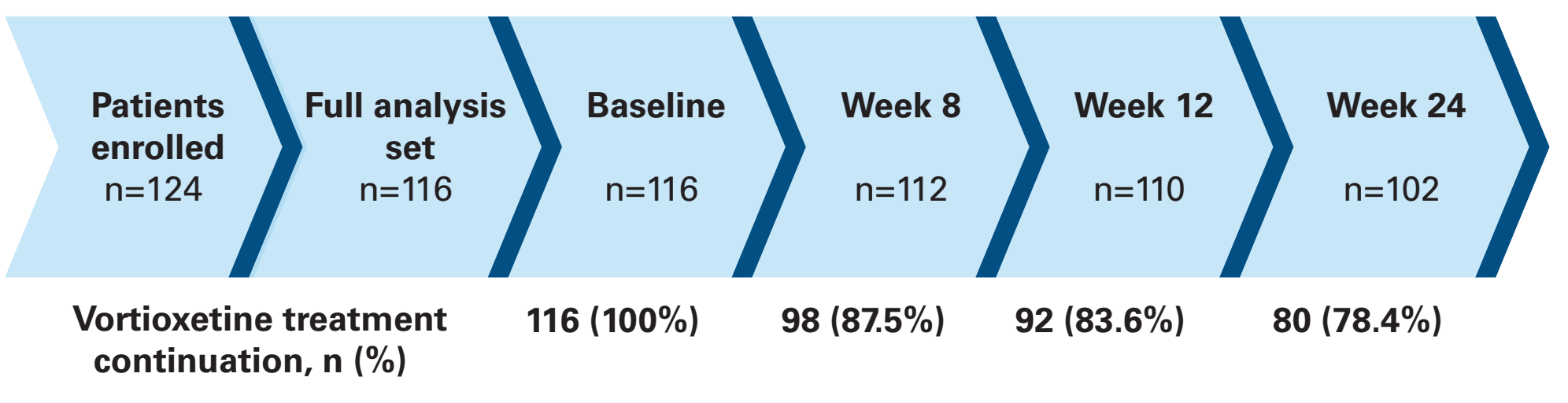
- The full analysis set (FAS) included all patients who gave informed consent, initiated vortioxetine treatment following the Japanese label, and completed the baseline visit and at least 1 follow-up visit
- Effectiveness analyses were performed on the FAS for both the primary and secondary endpoints
  - GAS-D goal-achievement rate was presented with a 95% CI calculated using the normal approximation interval. GAS-D score and the change from baseline were also presented with a mean (SD) and *P* value (2-sided)
  - The WPAI domains and secondary endpoint scales were analyzed based on a mixed effects model for repeated measurements, with age, sex, visits, baseline score, and baseline score-by-visit interaction as fixed effects

RESULTS

Patient Disposition

- A total of 124 patients were enrolled from 19 sites
  - The safety population included 121 patients who provided informed consent and initiated vortioxetine therapy; the FAS included 116 patients (**Figure 3**)
  - Overall, 103 patients completed the study; 21 were withdrawn from the trial due to consent decline (n=9), investigator's and sponsor's decision (n=7), lost to follow-up (n=4), or other reasons (n=1)

Figure 3. Patient Disposition and Vortioxetine Treatment Continuation



Baseline Characteristics

- Most patients (mean age 38 years) earned an associate's degree or higher (74%) and were working full- or part-time (66%), and 31% were employed but not working due to depression (**Table 1**)

Table 1. Baseline Demographics and Clinical Characteristics

Characteristics	N=116
Age in years, mean (SD)	38.4 (11.2)
Sex, female, n (%)	59 (50.9%)
Educational level, n (%)	
Junior high school or lower	4 (3.4%)
High school	26 (22.4%)
Diploma/associate's degree	37 (31.9%)
Bachelor's degree	39 (33.6%)
Master's degree	10 (8.6%)
Employment, n (%)	
Full-time or part-time	76 (65.5%)
Employed but not working due to depression	36 (31.0%)
Other	4 (3.4%)
Occupation, n (%)	
Manager/administrator	9 (7.8%)
Professional	14 (12.1%)
Associate professional	10 (8.6%)
Clerical work/secretary	25 (21.6%)
Skilled laborer/factory worker	7 (6.0%)
Services/sales	42 (36.2%)
Other	9 (7.8%)
History of MDD,* mean (SD)	
Number of years since first MDD diagnosis	5.8 (5.88)
Duration of current MDE, days	402.1 (727.63)
Number of previous MDEs	1.3 (1.39)
Treatment history	
Treatment-naïve	47 (40.5%)
Prior antidepressant	69 (59.5%)
SSRI	35 (50.7%)
Coadministered psychotropic medication	48 (41.4%)
Coadministered psychotherapy	2 (1.7%)

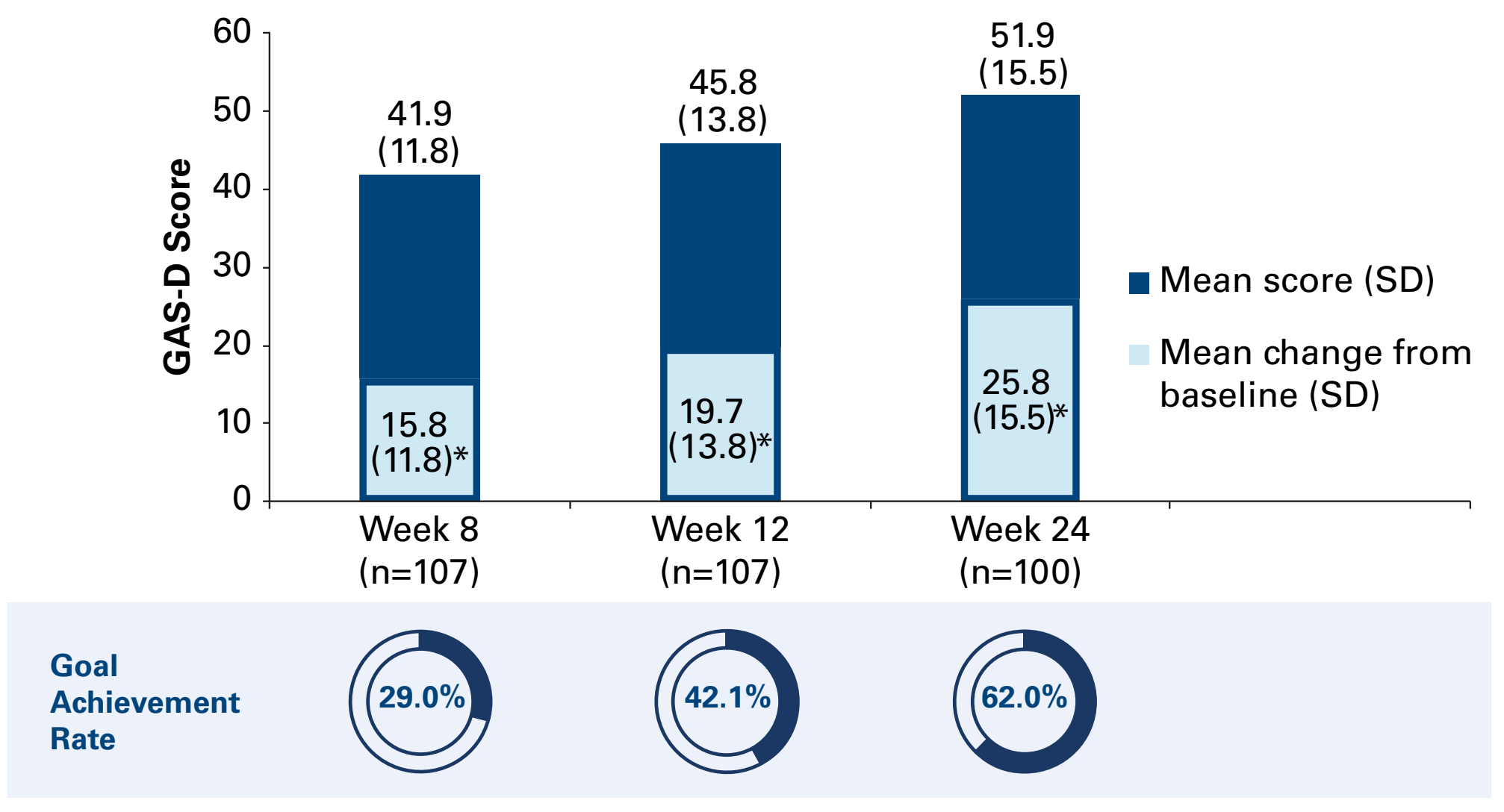
*10.3% of patients had psychiatric comorbidities.
MDD, major depressive disorder; MDE, major depressive episode; SSRI, selective serotonin reuptake inhibitor.

Clinical Outcomes Following Vortioxetine Treatment in a Real-World Setting

Primary outcomes

- Significant mean change (SD) in GAS-D scores vs baseline was observed at weeks 8 [15.8 (SD 11.8)], 12 [19.7 (SD 13.8)], and 24 [25.8 (15.5)]; *P*<0.001 for all (**Figure 4**)
- The proportion of patients overall achieving the preset goals on the GAS-D (95% CI) was 42.1% (33.1–52.1) at week 12 and increased to 62.0% (52.8–72.0) at week 24 (**Figure 4**)

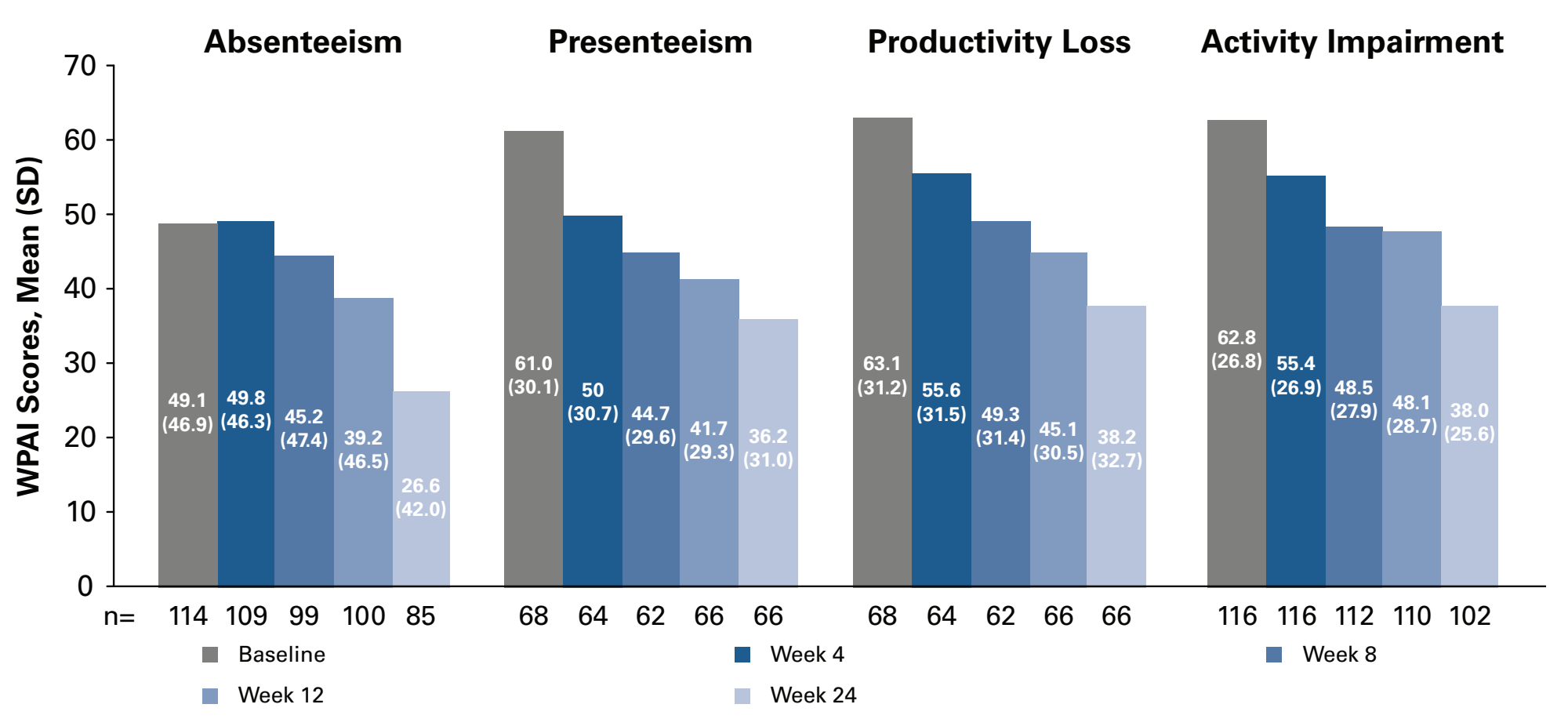
Figure 4. GAS-D Score, Change From Baseline, and Goal-Achievement Rate at Weeks 8, 12, and 24



*P<0.001.
"Goal Achievement" in each patient was defined as a standardized GAS-D score ≥50 (all goals achieved or exceeded overall).
GAS-D, Goal Attainment Scale-Depression.

- Significant improvements were observed in all WPAI domains from baseline to week 24 (*P*<0.001 for all) (**Figure 5**)

Figure 5. WPAI Scores From Baseline to Week 24

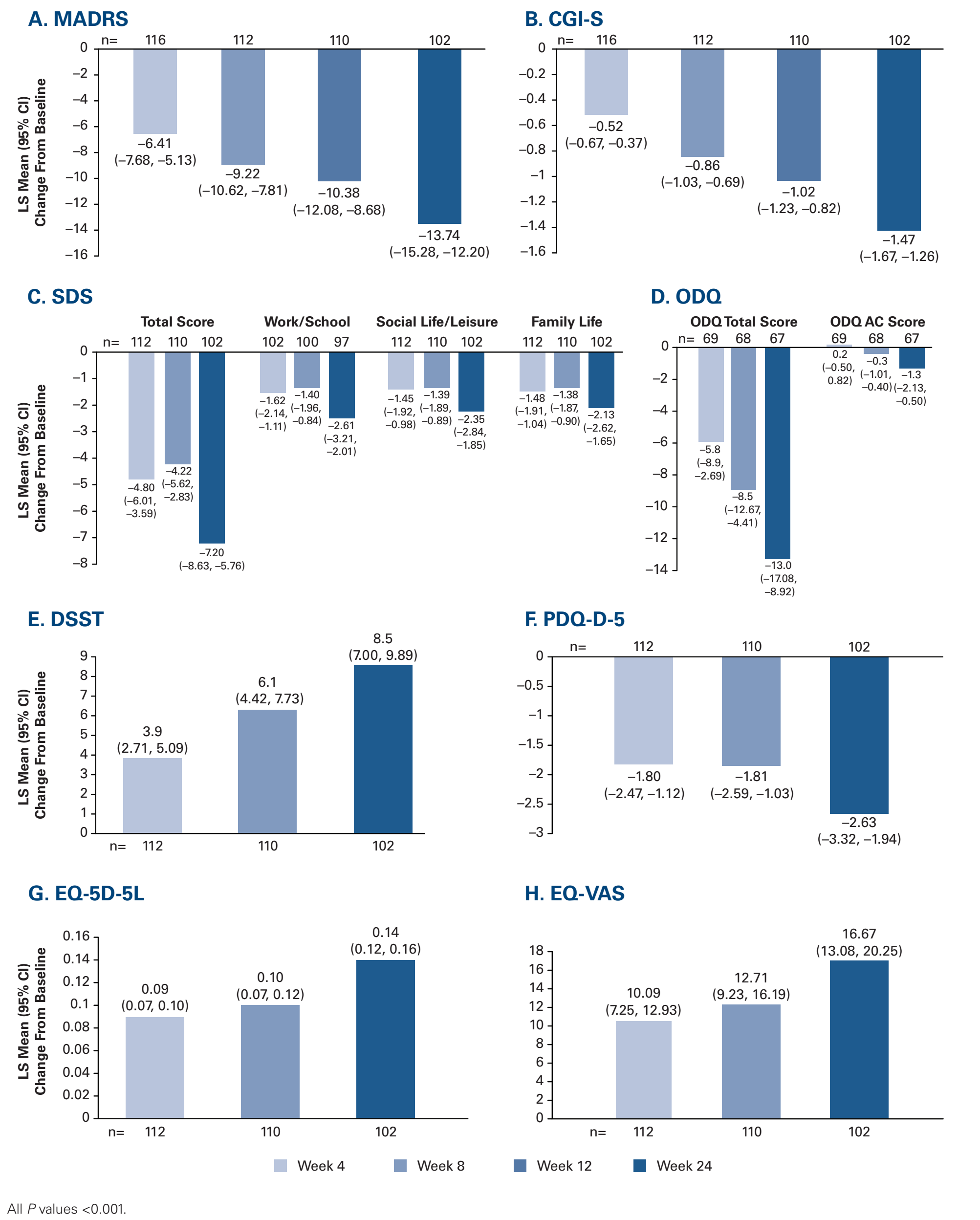


WPAI, Work Productivity and Activity Impairment questionnaire.

Secondary Outcomes

- Significant improvements were seen across all secondary endpoints and timepoints including depressive symptoms (MADRS and CGI-S), functioning (SDS), emotional symptoms (ODQ), cognitive symptoms (DSST and PDQ-D-5), and QoL (EQ-5D-5L and EQ-VAS) (**Figure 6**)
- SDS measures of work productivity were improved at weeks 8, 12, and 24
  - Mean reductions in absenteeism (SDS workdays lost) and presenteeism (SDS workdays underproductive) at week 24 were 1.5 and 1.7 days/week, respectively
- At 24 weeks, 52.0% of patients achieved remission based on MADRS total scores compared to 6% of patients at baseline (remission defined as MADRS total score of ≤10)
- Improvements in depressive symptom severity (CGI-C) and changes in health condition (PGI-C) were also observed at weeks 8, 12, and 24

Figure 6. Changes in Adjusted LS Mean Scores From Baseline to Weeks 8, 12, and 24 for Depressive Symptoms (A, B), Functioning (C), Emotional Symptoms (D), Cognitive Symptoms (E, F), and QoL (G, H)

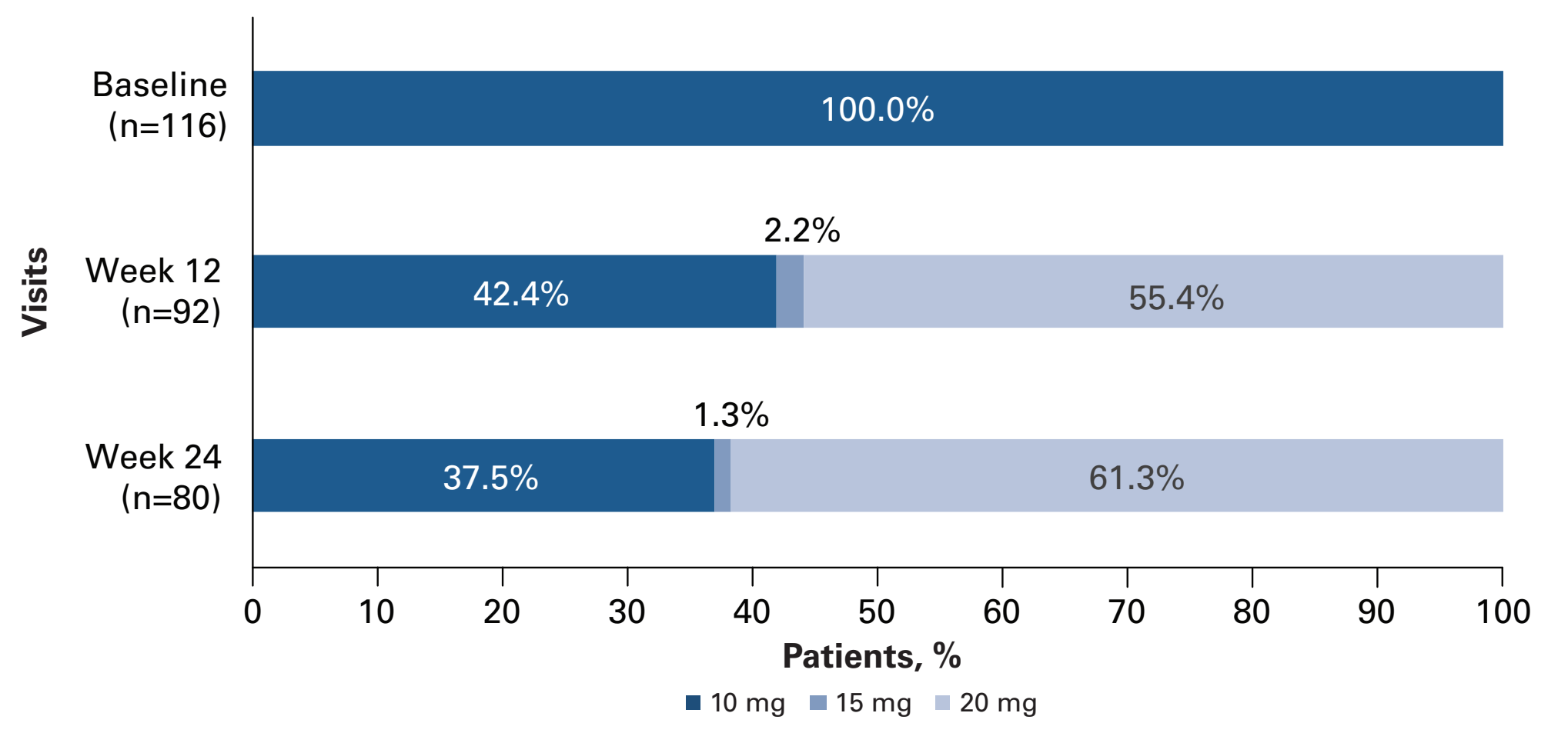


All *P* values <0.001.
AC, antidepressant as cause; CGI-S, Clinical Global Impressions–Severity; DSST, Digit Symbol Substitution Test; EQ-5D-5L, EuroQol Five Dimensions Five Levels; EQ-VAS, EuroQol Visual Analog Scale; LS, least squares; MADRS, Montgomery-Åsberg Depression Rating Scale; ODQ, Oxford Depression Questionnaire; PDQ-D-5, Perceived Deficits Questionnaire–Depression 5-item; QoL, quality of Life; SDS, Sheehan Disability Scale.

Vortioxetine Treatment Course

- At week 24, the majority of patients were prescribed vortioxetine at 20 mg daily (**Figure 7**)

Figure 7. Vortioxetine Dose at Baseline and Weeks 12 and 24



- One patient at week 4 and 2 patients at week 8 required dose reductions to 5 mg once daily (ie, one-half of a 10 mg tablet once daily), due to intolerance of higher doses
- At week 24, 89.2% of patients remained on antidepressant monotherapy; 10.8% were coadministered another antidepressant(s)

Healthcare Resource Utilization

- Throughout the course of the study, there were no emergency department visits, and only 5 hospitalization days were reported

Safety Analysis

- In total, 36.4% of patients reported at least one AE categorized as a "possible" or "probable" causality during the 24 weeks of vortioxetine treatment (**Table 2**); the majority of events related, or not related to vortioxetine were mild
- Radius fracture and suicide attempt were reported in 1 individual each as a severe and mild SAE, respectively; both were considered not related to the study drug

Table 2. Summary of Most Common AEs With Causality

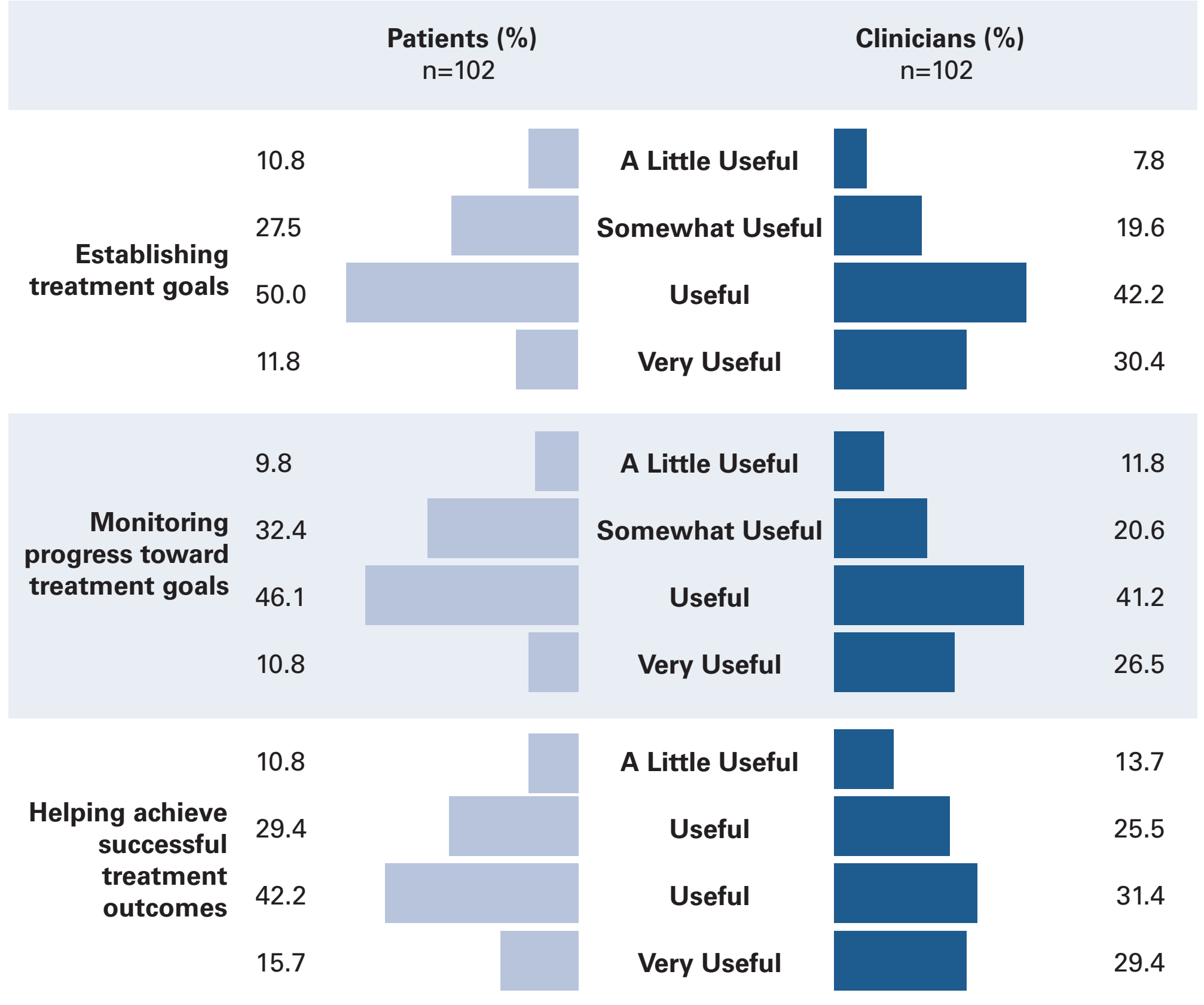
Preferred Term, n (%)	Mild	Moderate	Severe	Causality (–)	Causality (+)
At least one AE	53 (43.8%)	17 (14.0%)	1 (0.8%)	40 (33.1%)	44 (36.4%)
Nausea	19 (15.7%)	9 (7.4%)	-	2 (1.7%)	26 (21.4%)
Constipation	5 (4.1%)	-	-	2 (1.7%)	3 (2.5%)
Somnolence	6 (5.0%)	2 (1.7%)	-	4 (3.3%)	4 (3.3%)

AE, adverse event.

GAS-D Satisfaction Survey

- The majority of patients and clinicians reported the GAS approach to be "useful" or "very useful" for establishing treatment goals, monitoring progress toward treatment goals, and helping achieve successful treatment outcomes (**Figure 8**)
  - The proportion of clinicians finding the GAS approach "very useful" was higher than that of patients across categories

Figure 8. Patient and Clinician Satisfaction With the GAS-D Approach



CONCLUSIONS

- In this real-world study, the GAS-D, a patient-centered approach, was applied for the first time in Japan, which was reported as useful by both clinicians and patients
- It focused on the diversity of recovery of individual patients with MDD, addressing progress toward functional goal achievement in addition to alleviation of mood symptoms
- Patients initiated with vortioxetine treatment demonstrated:
  - Incremental improvements over time of both goal-achievement rates and scores on the GAS-D during the 24-week observation period
  - Continued improvements across all work productivity measures, including presenteeism and absenteeism
  - Improvements in depressive, cognitive, and emotional symptoms, overall functioning, and QoL
  - High continuation rate and low incidence of AEs
- Study data support the effectiveness and importance of longer-term treatment continuation initiated with vortioxetine to attain personal recovery for patients with MDD with continued employment

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DISCLOSURES

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