

## Supplemental tables

**Table e1.** Baseline characteristics.

**Table e2.** Changes in ODQ scores over 24 weeks.

**Table e3.** Multiple linear regression of baseline characteristics with ODQ scores and change from baseline of ODQ scores.

**Table e4.** Statistically significant correlations between ODQ scores and other clinical measures.

**Table e5.** Statistically significant correlations between change from baseline in ODQ and the changes in baseline in other clinical measures.

**Table e6.** Spearman correlation between ODQ Total score and sum of MADRS items related to emotional blunting across all visits.

**Table e1. Baseline characteristics (full analysis set)**

Characteristics	N=116
Age in years, mean (SD)	38.4 (11.2)
Sex, female, n (%)	59 (50.9%)
<b>History of MDD, mean (SD)</b>	
Years since first MDD diagnosis	5.8 (5.9)
Duration of current MDE, days	402 (728)
Number of previous MDEs	1.3 (1.4)
Prior suicide attempt, n (%)	6 (5.2%)

*MDE, major depressive episode*

**Table e2. Changes in ODQ scores over 24 weeks**

LS Mean [95% CI]	Week 8 (N=112)	Week 12 (N=110)	Week 24 (N=102)
ODQ Total	-5.8 [-8.9, -2.7] P<0.001	-8.5 [-12.7, -4.4] P<0.001	-13.0 [-17.1, -8.9] P<0.001
ODQ Section 1+2	-6.3 [-8.6, -4.0] P<0.001	-9.3 [-12.2, -6.4] P<0.001	-12.9 [-15.7, -10.1] P<0.001
ODQ General reduction	-1.0 [-1.7, -0.4] P<0.01	-2.0 [-2.7, -1.2] P<0.001	-2.6 [-3.4, -1.8] P<0.001
ODQ Positive reduction	-2.6 [-3.4, -1.8] P<0.001	-3.1 [-4.0, -2.2] P<0.001	-4.4 [-5.3, -3.5] P<0.001
ODQ Emotional detachment	-1.3 [-2.0, -0.6] P<0.001	-1.9 [-2.6, -1.2] P<0.001	-2.5 [-3.2, -1.8] P<0.001
ODQ Not caring	-1.3 [-2.0, -0.7] P<0.001	-2.3 [-3.1, -1.5] P<0.001	-3.4 [-4.2, -2.6] P<0.001
ODQ Antidepressant as cause	0.2 [-0.5, 0.8] NS	-0.3 [-1.0, -0.4] NS	-1.3 [-2.1, -0.5] P<0.01

*Results derived using a REML-based MMRM. The inferential model includes baseline age, sex, visit, baseline score, and baseline score by visit interaction as the fixed factors*

**Table e3. Multiple linear regression of baseline characteristics with ODQ scores and change from baseline of ODQ scores**

Baseline Characteristics	Week 12		Week 24	
	ODQ Total score $\beta$ [95% CI]	Change from Baseline $\beta$ [95% CI]	ODQ score $\beta$ [95% CI]	Change from Baseline $\beta$ [95% CI]
<b>Sample Size (n)</b>	<b>106</b>	<b>68</b>	<b>97</b>	<b>67</b>
Age (per year)	0.43 [0.00, 0.86]	0.22 [-0.27, 0.72]	0.41 [-0.07, 0.88]	0.27 [-0.24, 0.79]
Female vs. male	-0.08 [-8.82, 8.66]	1.91 [-7.79, 11.61]	3.02 [-6.40, 12.43]	6.05 [-3.76, 15.87]
Duration of current episode (per month)	0.04 [-0.14, 0.21]	0.03 [-0.15, 0.21]	0.00 [-0.19, 0.20]	0.02 [-0.16, 0.20]
Years since first MDD (per year)	0.51 [-0.36, 1.38]	-0.17 [-1.09, 0.74]	0.36 [-0.54, 1.26]	-0.25 [-1.18, 0.68]
Number of MDE (per episode)	-2.10 [-5.87, 1.68]	-2.89 [-6.56, 0.79]	-1.34 [-5.12, 2.44]	-1.70 [-5.35, 1.95]
Any suicidal attempts Yes vs. No	-9.36 [-27.59, 8.87]	-4.00 [-23.88, 15.88]	-3.37 [-21.48, 14.74]	2.97 [-16.98, 22.92]
Antidepressant prescribed before vortioxetine Yes vs. No	2.63 [-6.09, 11.35]	3.43 [-14.81, 21.67]	3.49 [-5.95, 12.94]	-1.92 [-20.31, 16.48]
MADRS total score (per SD)	7.94 [3.38, 12.51]	-2.30 [-6.94, 2.33]	7.87 [3.11, 12.63]	-2.91 [-7.58, 1.76]

**Table e4. Statistically significant correlations between ODQ scores and other clinical measures**

Measure	ODQ			
	Baseline	Week 8	Week 12	Week 24
WPAI Presenteeism	0.302	0.514	0.589	0.440
WPAI Productivity Loss	0.274 (NS)	0.452	0.580	0.468
WPAI Activity Impairment	0.454	0.517	0.627	0.578
MADRS Total Score	0.576	0.560	0.714	0.654
MADRS Anhedonia Factor Score	0.524	0.535	0.692	0.639
CGI-S Score	0.608	0.562	0.622	0.594
CGI-C Score	N/A	0.334	0.474	0.351
PGI-C	N/A	0.307	0.570	0.445
SDS Total Score	0.519	0.599	0.676	0.637
SDS Work/School Score	0.350	0.453	0.562	0.501
SDS Social life/leisure Score	0.491	0.588	0.662	0.662
SDS Family life Score	0.501	0.556	0.622	0.598
PDQ-D-5 Total Score	0.484	0.582	0.751	0.627
EQ-5D-5L Index Score	-0.482	-0.604	-0.573	-0.548
EQ VAS Score	-0.276	-0.552	-0.644	-0.549
DSST Score	-	-0.200	-0.372	-0.332

*Non-significant correlations not shown; N/A not applicable*

**Table e5. Statistically significant correlations between change from baseline in ODQ and the changes in baseline in other clinical measures**

Measure	ODQ		
	Week 8	Week 12	Week 24
WPAI Presenteeism	0.240	0.412	0.440
WPAI Productivity Loss	0.192	0.466	0.468
WPAI Activity Impairment	0.261	0.542	0.578
MADRS Total Score	0.400	0.611	0.654
MADRS Anhedonia Factor Score	0.414	0.572	0.639
CGI-S Score	0.426	0.638	0.594
SDS Total Score	0.284	0.458	0.637
SDS Work/School Score	0.262	0.285	0.501
SDS Social life/leisure Score	0.246	0.392	0.662
SDS Family life Score	-	0.421	0.598
PDQ-D-5 Total Score	0.280	0.447	0.627
EQ-5D-5L Index Score	-0.296	-0.445	-0.548
EQ VAS Score	-0.266	-0.448	-0.549
DSST Score	-	-	-0.332

*Non-significant correlations not shown.*

**Table e6. Spearman correlation between ODQ Total score and sum of MADRS items related to emotional blunting across all visits**

MADRS Items	Spearman Coefficient	P value
[8] Inability to Feel + [6] Concentration Difficulties	0.611	p<0.001
[8] Inability to Feel + [6] Concentration Difficulties + [7] Lassitude	0.620	p<0.001
[8] Inability to Feel + [6] Concentration Difficulties + [4] Reduced Sleep	0.631	p<0.001
[8] Inability to Feel + [6] Concentration Difficulties + [7] Lassitude + [4] Reduced Sleep	0.646	p<0.001