

Supplementary Material

Article Title: Impact of Vagus Nerve Stimulation on Suicidal Ideation in Markedly Treatment-Resistant Major Depression: A RECOVER Study Report

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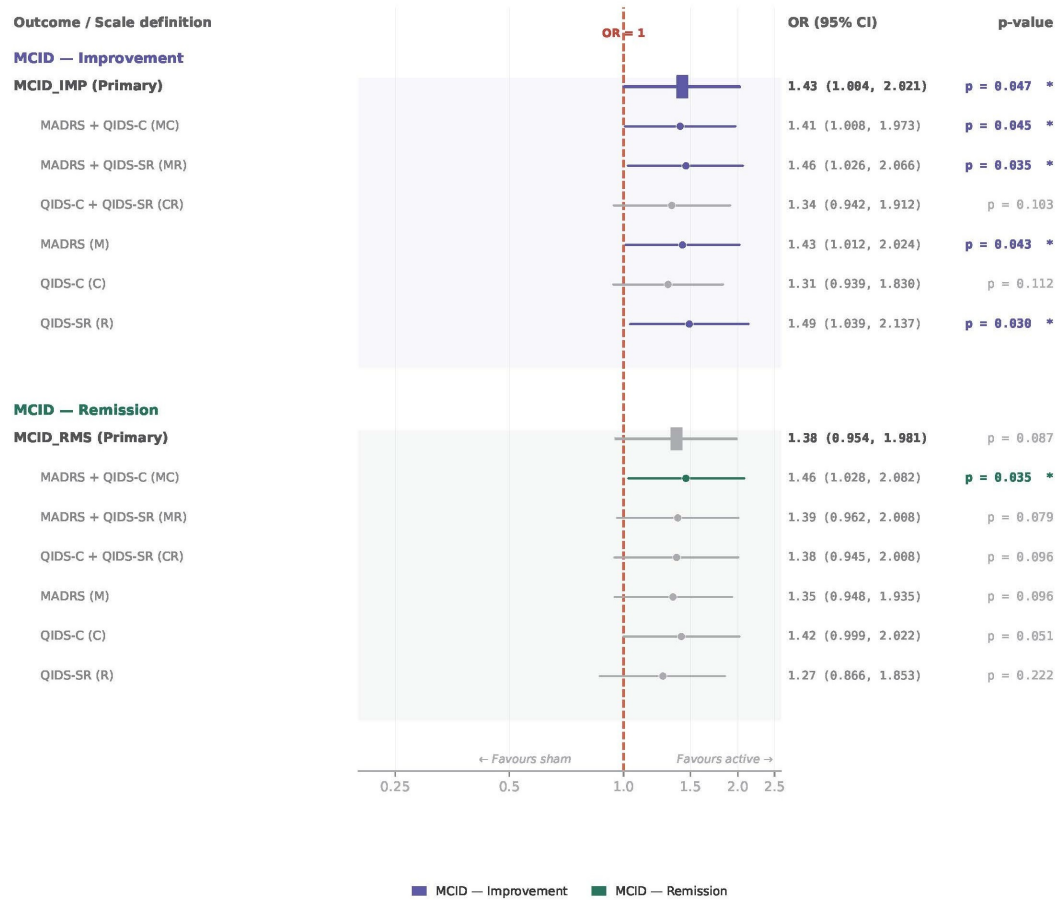
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DISCLAIMER

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Supplementary Figure 1. Forest plot showing odds ratio of achieving improvement or remission with active versus sham VNS from months 3 to 12 in participants with CSI ≥ 3 (N=286).



Abbreviations: CI, confidence interval; CSI, composite suicidal ideation; IMP, improvement; MADRS, Montgomery-Åsberg Depression Rating Scale; MCID, minimal clinically important difference; OR, odds ratio; QIDS-C, Quick Inventory of Depressive Symptomatology–Clinician; QIDS-SR, Quick Inventory of Depressive Symptomatology–Self-Report; RMS, remission; VNS, vagus nerve stimulation.

Supplementary Table 1. Degree of SI by each measure and composite (CSI) at baseline in participants with (CSI ≥ 3) and without (CSI < 3) meaningful SI receiving active and sham VNS.

	Active VNS N=234	Sham VNS N=229	P Value^a (t-test or chi-square)
Participants With Baseline CSI ≥ 3, n (%)^b	145 (62.0%)	141 (61.6%)	
Adjusted MADRS item 10 (0–3)			
Mean (SD)	1.65 (0.61)	1.67 (0.54)	<i>P</i> =0.79
Median (Q1, Q3)	2.00 (1.00, 3.00)	2.00 (1.00, 3.00)	
QIDS-C item 12 (0–3)			
Mean (SD)	1.50 (0.68)	1.50 (0.65)	<i>P</i> =0.99
Median (Q1, Q3)	1.00 (1.00, 2.00)	1.00 (1.00, 2.00)	
QIDS-SR item 12 (0–3)			
Mean (SD)	1.52 (0.69)	1.45 (0.60)	<i>P</i> =0.34
Median (Q1, Q3)	1.00 (1.00, 2.00)	1.00 (1.00, 2.00)	
CSI ^c (0–9)			
Mean (SD)	4.67 (1.63)	4.62 (1.43)	<i>P</i> =0.79

Median (Q1, Q3)	4.00 (3.00, 6.00)	4.00 (3.00, 6.00)	
By (CSI), n (%)			
Score 0–2 (minimal SI)	NA ^d	NA ^d	
Score 3–4 (mild SI)	79 (54.5%)	73 (51.8%)	<i>P</i> =0.59
Score 5–6 (moderate SI)	49 (33.8%)	55 (39.0%)	
Score 7–9 (severe SI)	17 (11.7%)	13 (9.2%)	
Participants With CSI <3, n (%)^b	89 (38.0%)	88 (38.4%)	
Transformed MADRS item 10 (0–3)			
Mean (SD)	0.31 (0.47)	0.50 (0.50)	<i>P</i>=0.01
Median (Q1, Q3)	0.00 (0.00, 1.00)	0.50 (0.00, 1.00)	
QIDS-C item 12 (0–3)			
Mean (SD)	0.17 (0.38)	0.26 (0.44)	<i>P</i> =0.13
Median (Q1, Q3)	0.00 (0.00, 1.00)	0.00 (0.00, 1.00)	
QIDS-SR item 12 (0–3)			
Mean (SD)	0.22 (0.52)	0.29 (0.48)	<i>P</i> =0.41
Median (Q1, Q3)	0.00 (0.00, 2.00)	0.00 (0.00, 1.00)	

CSI (0–9)			
Mean (SD)	0.71 (0.89)	1.05 (0.87)	P=0.01
Median (Q1, Q3)	0.00 (0.00, 2.00)	1.00 (0.00, 2.00)	

Bolded *P* values indicate clinical significance.

*Denotes statistically significant result.

^a*P* values from Pearson's chi-square for categorical variables and *t* test for continuous variables were generated independently for each variable between active VNS vs sham VNS.

^bRepresents proportion from the total sample within each treatment group.

^cRepresents active SI.

^dNA: This population requires a baseline CSI score ≥ 3 .

Abbreviations: CSI, composite suicidal ideation; MADRS, Montgomery-Åsberg Depression Rating Scale; NA, not applicable; Q1, lower quartile; Q3, upper quartile; QIDS-C, Quick Inventory of Depressive Symptomatology–Clinician; QIDS-SR, Quick Inventory of Depressive Symptomatology–Self-Report; SD, standard deviation; SI, suicidal ideation; VNS, vagus nerve stimulation.

Supplementary Table 2. Month-by-month comparison of percentage of participants with CSI ≥ 3 achieving meaningful improvement or resolution of suicidal ideation.

	M3	M4	M5	M6	M7	M8	M9	M10	M11	M12
Meaningful Improvement^a										
Active VNS (N=145)	44.4% (64/144)	47.1% (66/140)	47.4% (64/135)	49.3% (68/138)	51.5% (68/132)	56.0% (75/134)	53.7% (72/134)	49.6% (66/133)	51.5% (68/132)	57.2% (79/138)
Sham VNS (N=141)	36.6 % (49/134)	36.0% (49/136)	38.5% (52/135)	40.5% (53/131)	42.6% (55/129)	40.8% (53/130)	45.3% (58/128)	39.8% (51/128)	48.1% (62/129)	49.6% (66/133)
Remission^b										
Active VNS (N=145)	38.9% (56/144)	40.7% (57/140)	43.0% (58/135)	39.9% (55/138)	44.7% (59/132)	50.0% (67/134)	48.5% (65/134)	44.4% (59/133)	49.2% (65/132)	49.3% (68/138)
Sham VNS (N=141)	32.8% (44/134)	33.1% (45/136)	34.1% (46/135)	35.9% (47/131)	34.9% (45/129)	36.9% (48/130)	39.1% (50/128)	36.7% (47/128)	42.6% (55/129)	45.1% (60/133)

^aMeaningful improvement is defined as a reduction in CSI score ≥ 3 .

^bRemission in suicidal ideation is defined as a CSI score of 0, 1, or 2 and at least a 3-point CSI reduction from baseline.

Abbreviations: CSI, composite suicidal ideation; M, month; VNS, vagus nerve stimulation.