

Supplemental Data

Table S1. Participants Currently Taking ADTs for at Least 6 Weeks During the Current MDE (Safety Population)

Antidepressant Treatment	Placebo (N=253)		Cariprazine 1.5 mg/d (N=252)		Cariprazine 3.0 mg/d (N=252)	
	N	%	N	%	N	%
Clomipramine						
At minimum dosage or above	3	1.2	1	0.4	1	0.4
Dose escalated at least once	2	0.8	1	0.4	1	0.4
Vortioxetine						
At minimum dosage or above	5	2.0	8	3.2	11	4.4
Dose escalated at least once	5	2.0	5	2.0	10	4.0
Citalopram						
At minimum dosage or above	18	7.1	12	4.8	19	7.5
Dose escalated at least once	16	6.3	12	4.8	19	7.5
Duloxetine						
At minimum dosage or above	25	9.9	29	11.5	28	11.1
Dose escalated at least once	23	9.1	28	11.1	26	10.3
Trazodone						
At minimum dosage or above	3	1.2	4	1.6	4	1.6
Dose escalated at least once	3	1.2	3	1.2	2	0.8
Venlafaxine						
At minimum dosage or above	29	11.5	43	17.1	28	11.1
Dose escalated at least once	29	11.5	39	15.5	26	10.3
Amitriptyline						
At minimum dosage or above	5	2.0	4	1.6	1	0.4
Dose escalated at least once	5	2.0	4	1.6	1	0.4
Escitalopram						
At minimum dosage or above	58	22.9	53	21.0	55	21.8
Dose escalated at least once	55	21.7	51	20.2	50	19.8
Desipramine						
At minimum dosage or above	1	0.4	0	0.0	0	0.0
Dose escalated at least once	1	0.4	0	0.0	0	0.0
Mianserin						
At minimum dosage or above	4	1.6	4	1.6	4	1.6
Dose escalated at least once	4	1.6	4	1.6	4	1.6
Paroxetine						
At minimum dosage or above	17	6.7	19	7.5	19	7.5
Dose escalated at least once	17	6.7	18	7.1	17	6.7
Desvenlafaxine						
At minimum dosage or above	1	0.4	2	0.8	3	1.2
Dose escalated at least once	1	0.4	2	0.8	3	1.2
Fluoxetine						
At minimum dosage or above	24	9.5	27	10.7	25	9.9
Dose escalated at least once	23	9.1	25	9.9	24	9.5
Mirtazapine						
At minimum dosage or above	10	4.0	16	6.3	7	2.8
Dose escalated at least once	9	3.6	13	5.2	7	2.8
Doxepin						
At minimum dosage or above	1	0.4	0	0.0	0	0.0

Dose escalated at least once	1	0.4	0	0.0	0	0.0
Trimipramine						
At minimum dosage or above	0	0.0	0	0.0	1	0.4
Dose escalated at least once	0	0.0	0	0.0	1	0.4
Imipramine						
At minimum dosage or above	1	0.4	0	0.0	0	0.0
Dose escalated at least once	1	0.4	0	0.0	0	0.0
Agomelatine						
At minimum dosage or above	6	2.4	1	0.4	6	2.4
Dose escalated at least once	6	2.4	0	0.0	6	2.4
Vilazodone						
At minimum dosage or above	3	1.2	4	1.6	3	1.2
Dose escalated at least once	3	1.2	3	1.2	3	1.2
Bupropion						
At minimum dosage or above	22	8.7	17	6.7	17	6.7
Dose escalated at least once	21	8.3	16	6.3	16	6.3
Sertraline						
At minimum dosage or above	53	20.9	43	17.1	52	20.6
Dose escalated at least once	49	19.4	40	15.9	50	19.8

Based on Antidepressant Treatment Response Questionnaire (ATRQ).

Table S2. Participants (n, %) With Treatment-Emergent Significant Changes in Lipids and Glucose During the Double-Blind Treatment Phase (Safety Population)

Clinical Laboratory Parameter	Baseline (mg/dL)	Postbaseline (mg/dL)	Placebo (N=253)		Cariprazine 1.5 mg/d (N=252)		Cariprazine 3.0 mg/d (N=252)	
			n/N1	(%)	n/N1	%	n/N1	%
Cholesterol, total								
Normal to high	<200	≥240	1/93	1.1	0/121	—	2/114	1.8
Borderline to high	≥200 and <240	≥240	12/74	16.2	8/77	10.4	7/75	9.3
Normal/borderline to high	<240	≥240	13/167	7.8	8/198	4.0	9/189	4.8
Normal to borderline/high	<200	≥200	18/93	19.4	19/121	15.7	14/114	12.3
Combined LDL direct and calculated, fasting								
Normal to high	<100	≥160	0/46	—	0/66	—	0/60	—
Borderline to high	≥100 and <160	≥160	14/115	12.2	10/117	8.5	7/104	6.7
Normal/borderline to high	<160	≥160	14/161	8.7	10/183	5.5	7/164	4.3
Normal to borderline/high	<100	≥100	11/46	23.9	6/66	9.1	7/60	11.7
Cholesterol HDL								
Normal to low	≥40	<40	9/192	4.7	7/204	3.4	14/214	6.5
Triglycerides, fasting								
Normal to high	<150	≥200	9/135	6.7	10/148	6.8	8/148	5.4
Normal to very high	<150	≥500	0/135	—	0/148	—	0/148	—
Borderline to high	≥150 and <200	≥200	11/36	30.6	9/29	31.0	3/21	14.3
Borderline to very high	≥150 and <200	≥500	0/36	—	0/29	—	0/21	—
Normal/borderline to high	<200	≥200	20/171	11.7	19/177	10.7	11/169	6.5
Normal/borderline to very high	<200	≥500	0/171	—	0/177	—	0/169	—
Normal to borderline/high/very high	<150	≥150	26/135	19.3	22/148	14.9	26/148	17.6
Treatment-emergent triglycerides								
Treatment-emergent very high, fasting	<500	≥500	1/205	0.5	0/205	—	2/201	1.0
Treatment-emergent very high, nonfasting and random	<500	≥500	0/8	—	0/6	—	1/12	8.3
Treatment-emergent >1000 mg/dL (all cases)	<1000	≥1000	0/213	—	0/212	—	0/215	—
Change in cholesterol								
Change in fasting or nonfasting total cholesterol ≥40 mg/dL	Any value	Increase ≥40	10/231	4.3	9/235	3.8	13/237	5.5
Change in fasting LDL cholesterol ≥30 mg/dL	Any value	Increase ≥30	13/204	6.4	12/207	5.8	11/200	5.5
Change in fasting or nonfasting HDL cholesterol ≥20 mg/dL	Any value	Decrease ≥20	6/231	2.6	7/235	3.0	4/236	1.7
Change in fasting triglycerides ≥50 mg/dL	Any value	Increase ≥50	32/205	15.6	30/206	14.6	33/203	16.3

N=total number of participants in the Safety Population; N1=number of participants with baseline meeting the baseline criteria and with at least one nonmissing postbaseline value during the double-blind treatment period; n=number of patients who met the criterion; HDL=high-density lipoprotein; LDL=low-density lipoprotein.