

Supplementary Material

Article Title: Cariprazine for the Adjunctive Treatment of Major Depressive Disorder in Patients With Inadequate Response to Antidepressant Therapy: Results of a Randomized, Double-Blind, Placebo-Controlled Study

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SUPPLEMENTARY MATERIALS

Supplementary Table 1. Mean Changes in Safety Parameters During Double-Blind Treatment Period (Safety Population)^a

	n	Placebo + ADT (n=250)	n	Cariprazine		
				1.5 mg/d + ADT (n=250)	3 mg/d + ADT (n=251)	
Metabolic parameters, mean change (SD)						
Total cholesterol, mg/dL	233	-2.8 (28.96)	239	0.5 (28.16)	239	-3.8 (28.34)
LDL cholesterol, mg/dL	196	-4.0 (25.17)	205	-3.7 (24.20)	202	-6.4 (25.61)
HDL cholesterol, mg/dL	232	-0.3 (8.34)	239	0.8 (9.73)	239	0.3 (8.74)
Fasting triglycerides, mg/dL	197	8.9 (62.21)	205	14.0 (66.70)	202	15.1 (57.06)
Fasting glucose, mg/dL	197	1.4 (14.09)	205	0.6 (16.17)	202	4.1 (16.50)
Prolactin, mean change (SD)						
Prolactin, ng/mL	233	0.92 (14.130)	238	3.79 (7.940)	237	2.91 (10.673)
Liver tests, mean change (SD)						
Alkaline phosphatase, U/L	232	0.8 (10.86)	238	0.6 (12.05)	238	0.5 (10.92)
ALT, U/L	230	0.2 (10.41)	237	4.8 (40.28)	233	1.6 (8.83)
AST, U/L	232	0.1 (6.95)	234	3.1 (21.86)	231	0.7 (7.41)
Total bilirubin, mg/dL	229	-0.02 (0.164)	236	-0.01 (0.342)	238	-0.05 (0.164)
Vital signs, mean change (SD)						
Systolic blood pressure, mmHg	248	0.0 (9.44)	249	-1.4 (9.51)	251	-0.9 (10.01)
Diastolic blood pressure, mmHg	248	-0.1 (7.14)	249	0.2 (7.08)	251	-0.4 (7.54)
Pulse, bpm	248	-1.6 (8.75)	247	-0.5 (8.69)	248	-0.3 (8.98)
Body weight, kg	248	0.20 (1.649)	249	0.68 (2.021)	251	0.66 (2.023)
BMI, kg/m ²	248	0.06 (0.610)	249	0.25 (0.725)	251	0.24 (0.727)
Orthostatic hypotension, n (%) ^b	237	23 (9.7)	244	21 (8.6)	241	28 (11.6)
Electrocardiogram, mean change (SD)						
Ventricular heart rate, bpm	237	2.9 (9.17)	242	3.3 (9.97)	238	2.2 (9.77)
PR interval, msec	237	-1.6 (11.42)	241	-2.4 (13.15)	237	-0.9 (13.41)
QRS interval, msec	237	0.0 (7.74)	242	-0.5 (6.85)	238	-0.5 (6.92)
QT interval, msec	237	-6.2 (19.50)	242	-7.7 (24.24)	238	-5.9 (23.53)
QTcB interval, msec	237	2.3 (19.29)	242	1.3 (18.15)	238	0.0 (18.26)
QTcF interval, msec	237	-0.7 (14.80)	242	-1.9 (15.98)	238	-2.1 (16.01)

^aPatients with non-missing analysis values at both baseline and postbaseline during the analysis visit.

^bOrthostatic hypotension defined as a reduction of ≥ 20 mmHg in systolic blood pressure or a reduction of ≥ 10 mmHg in diastolic blood pressure while changing from supine position to the standing position.

ADT, antidepressant therapy; ALT, alanine aminotransferase; AST, aspartate aminotransferase; AE, adverse event; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TEAE, treatment-emergent AE.

Supplementary Table 2. Participants 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 + ADT (N = 250) n/N1 (%)	Cariprazine	
				1.5 mg/d + ADT (N = 250) n/N1 (%)	3.0 mg/d + ADT (N = 251) n/N1 (%)
Cholesterol, total					
Normal to high	<200	≥240	3/110 (2.7)	4/125 (3.2)	2/110 (1.8)
Borderline to high	≥200 and <240	≥240	9/72 (12.5)	14/71 (19.7)	13/74 (17.6)
Normal/borderline to high	<240	≥240	12/182 (6.6)	18/196 (9.2)	15/184 (8.2)
Normal to borderline/high	<200	≥200	22/110 (20.0)	20/125 (16.0)	13/110 (11.8)
Combined LDL direct and calculated, fasting					
Normal to high	<100	≥160	0/52 (0.0)	2/68 (2.9)	1/64 (1.6)
Borderline to high	≥100 and <160	≥160	10/111 (9.0)	7/107 (6.5)	4/96 (4.2)
Normal/borderline to high	<160	≥160	10/163 (6.1)	9/175 (5.1)	5/160 (3.1)
Normal to borderline/high	<100	≥100	17/52 (32.7)	12/68 (17.6)	12/64 (18.8)
Cholesterol HDL					
Normal to low	≥40	<40	15/209 (7.2)	13/217 (6.0)	7/214 (3.3)
Triglycerides, fasting					
Normal to high	<150	≥200	8/139 (5.8)	10/140 (7.1)	10/148 (6.8)
Normal to very high	<150	≥500	0/139 (0.0)	0/140 (0.0)	0/148 (0.0)
Borderline to high	≥150 and <200	≥200	7/33 (21.2)	11/39 (28.2)	10/31 (32.3)
Borderline to very high	≥150 and <200	≥500	0/33 (0.0)	0/39 (0.0)	0/31 (0.0)
Normal/borderline to high	<200	≥200	15/172 (8.7)	21/179 (11.7)	20/179 (11.2)
Normal/borderline to very high	<200	≥500	0/172 (0.0)	0/179 (0.0)	0/179 (0.0)
Normal to borderline/high/very high	<150	≥150	33/139 (23.7)	26/140 (18.6)	28/148 (18.9)
Treatment-emergent triglycerides					
Treatment-emergent very high, fasting	<500	≥500	1/195 (0.5)	2/204 (1.0)	0/201 (0.0)
Treatment-emergent very high, nonfasting and random	<500	≥500	0/10 (0.0)	0/6 (0.0)	0/17 (0.0)

Treatment-emergent >1000 mg/dL (all cases)	<1000	≥1000	0/207 (0.0)	0/211 (0.0)	0/219 (0.0)
Change in cholesterol					
Change in fasting or nonfasting total cholesterol ≥40 mg/dL	Any value	Increase ≥40	15/233 (6.4)	19/239 (7.9)	12/239 (5.0)
Change in fasting LDL cholesterol ≥ 30 mg/dL	Any value	Increase ≥30	15/196 (7.7)	19/205 (9.3)	13/202 (6.4)
Change in fasting or nonfasting HDL cholesterol ≥20 mg/dL	Any value	Decrease ≥20	5/232 (2.2)	4/239 (1.7)	3/239 (1.3)
Change in fasting triglycerides ≥50 mg/dL	Any value	Increase ≥50	34/197 (17.3)	38/205 (18.5)	38/202 (18.8)
Change in glucose, fasting					
Normal to high	<100	≥126	1/151 (0.7)	2/143 (1.4)	5/155 (3.2)
Impaired to high	≥100 and <126	≥126	3/41 (7.3)	3/54 (5.6)	3/44 (6.8)
Normal/impaired to high	<126	≥126	4/192 (2.1)	5/197 (2.5)	8/199 (4.0)
Normal to impaired	<100	≥100 and <126	30/151 (19.9)	15/143 (10.5)	33/155 (21.3)
Change ≥10 mg/dL	Any value	Increase ≥10	37/197 (18.8)	31/205 (15.1)	48/202 (23.8)
Change in glucose, nonfasting					
Normal to high	<140	≥200	0/10 (0.0)	0/6 (0.0)	0/16 (0.0)
Impaired to high	≥140 and <200	≥200	0/0	0/0	0/0
Normal/impaired to high	<140	≥140	0/10 (0.0)	0/6 (0.0)	1/16 (6.3)
Normal to impaired	<200	≥200	0/10 (0.0)	0/6 (0.0)	0/6 (0.0)
Change ≥20 mg/dL	Any value	Increase ≥20	0/10 (0.0)	1/6 (16.7)	3/17 (17.6)

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.