Data Supplement for Earley et al., Cariprazine Treatment of Bipolar Depression: A Randomized Double-Blind Placebo-Controlled Phase 3 Study. Am J Psychiatry (doi: 10.1176/appi.ajp.2018.18070824)

**TABLE S1.** Incidence of extrapyramidal symptoms-related TEAEs by treatment group and preferred term, double-blind treatment period (safety population)

| Preferred Term | Placebo (n=158) n (%) | Cariprazine 1.5 mg/d (n=157) n (%) | Cariprazine 3.0 mg/d (n=165) n (%) |
|---|---|---|---|
| Patients with at least one EPS TEAE | 13 (8.2) | 17 (10.8) | 26 (15.8) |
| Restlessness | 6 (3.8) | 2 (1.3) | 12 (7.3) |
| Akathisia | 5 (3.2) | 10 (6.4) | 9 (5.5) |
| Musculoskeletal stiffness | 0 | 0 | 2 (1.2) |
| Salivary hypersecretion | 1 (0.6) | 4 (2.5) | 1 (0.6) |
| Tremor | 2 (1.3) | 1 (0.6) | 1 (0.6) |
| Muscle tightness | 0 | 1 (0.6) | 1 (0.6) |
| Extrapyramidal disorder | 1 (0.6) | 0 | 1 (0.6) |
| Tardive dyskinesia | 0 | 0 | 1 (0.6) |
| Drooling | 0 | 1 (0.6) | 0 |
| Oculogyric crisis | 1 (0.6) | 0 | 0 |

n=number of patients with EPS TEAEs

Patients are counted only once within each preferred term.

AEs that occurred more than 30 days after the last dose of double-blind investigational product are not included in the summary.

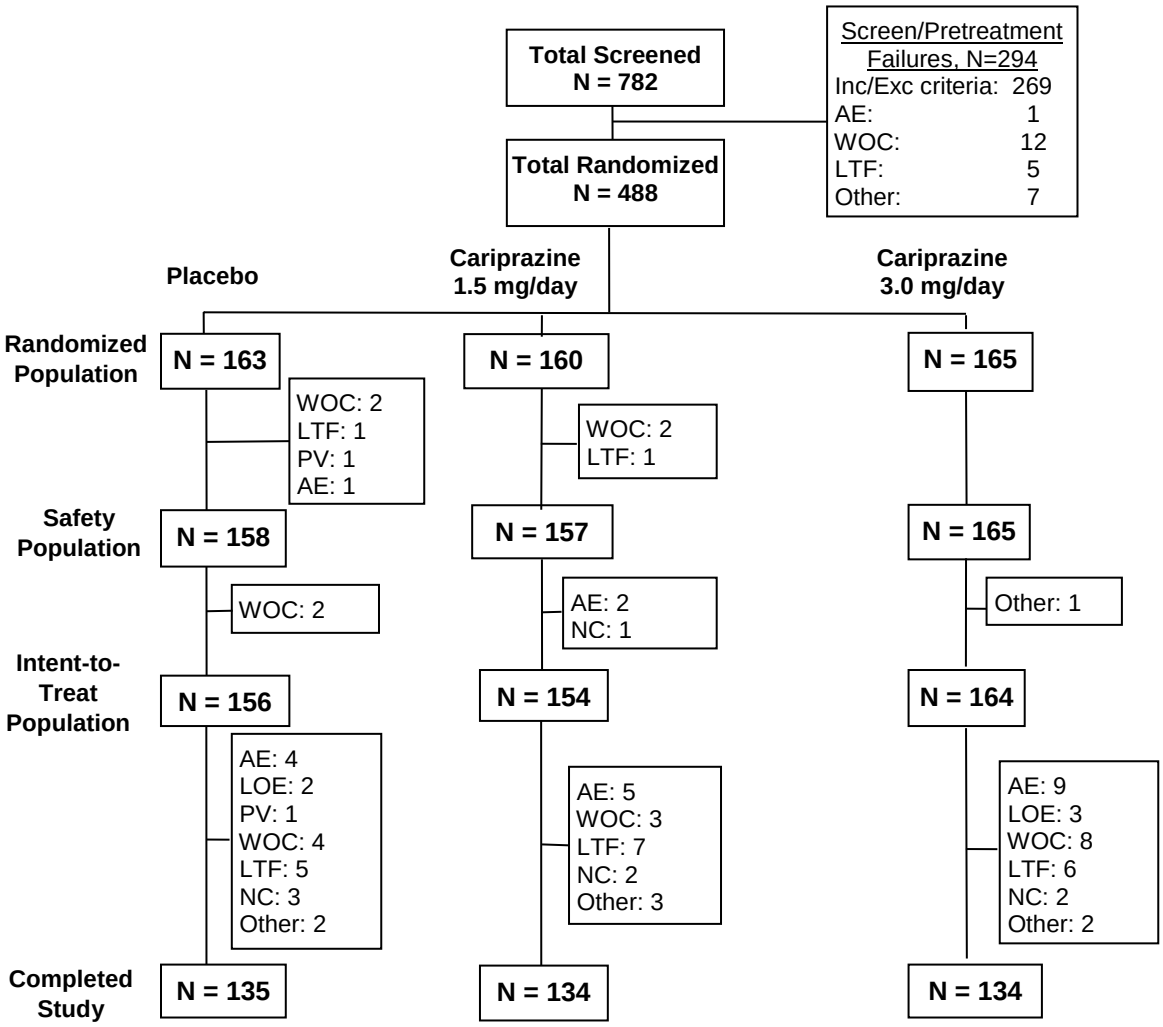
**TABLE S2.** Changes from baseline in clinical laboratory values

| Parameter | Placebo | | | Cariprazine 1.5 mg/d | | | Cariprazine 3.0 mg/d | | |
|---|---|---|---|---|---|---|---|---|---|
| | N | Mean | SD | N | Mean | SD | N | Mean | SD |
| **Liver Function** | | | | | | | | | |
| Alanine aminotransferase, U/L | 149 | 0.5 | 10.1 | 148 | 0.1 | 7.3 | 152 | 2.5 | 15.9 |
| Aspartate aminotransferase, U/L | 149 | 0.4 | 10.5 | 148 | -0.4 | 6.4 | 152 | 0.6 | 8.5 |
| Total bilirubin, mg/dL | 148 | 0.023 | 0.196 | 148 | -0.021 | 0.281 | 152 | -0.011 | 0.191 |
| **Metabolic Parameters** | | | | | | | | | |
| HDL cholesterol, mg/dL | 149 | 1.28 | 9.84 | 148 | -0.46 | 11.08 | 152 | -1.30 | 8.53 |
| LDL cholesterol, mg/dL[a] | 149 | -4.17 | 21.10 | 148 | -5.95 | 23.50 | 152 | -6.72 | 24.49 |
| Total cholesterol, mg/dL | 149 | -3.46 | 26.24 | 148 | -4.46 | 26.68 | 152 | -6.90 | 26.93 |
| Triglycerides, mg/dL | 132 | -3.22 | 52.46 | 125 | 9.86 | 57.16 | 129 | 4.81 | 54.69 |
| Fasting glucose, mg/dL | 132 | 3.35 | 11.90 | 126 | 5.04 | 23.73 | 127 | 2.69 | 12.44 |
| **Chemistry Parameters** | | | | | | | | | |
| Prolactin, ng/mL | 137 | -1.11 | 13.75 | 136 | -1.23 | 26.97 | 136 | 2.14 | 12.50 |
| Creatine kinase, U/L | 149 | 13.2 | 88.9 | 148 | 14.1 | 130.5 | 152 | 20.6 | 92.0 |
| **Vital Signs** | | | | | | | | | |
| Systolic blood pressure, mmHg[b] | 158 | -0.3 | 9.8 | 157 | -0.2 | 10.8 | 165 | -0.5 | 10.9 |
| Diastolic blood pressure, mmHg[b] | 158 | 0.2 | 8.1 | 157 | -0.6 | 7.9 | 165 | -0.5 | 7.0 |
| Pulse rate, bpm[b] | 158 | -0.50 | 9.2 | 157 | -1.0 | 10.6 | 165 | 1.8 | 9.0 |
| Body weight, kg | 158 | -0.27 | 2.31 | 157 | 0.48 | 1.85 | 165 | 0.45 | 2.20 |
| Waist circumference, cm | 156 | -0.73 | 3.84 | 151 | -0.08 | 3.52 | 161 | 0.41 | 3.34 |
| **Other Safety Outcomes** | **n/N1[c]** | | **%** | **n/N1[c]** | | **%** | **n/N1[c]** | | **%** |
| Orthostatic hypotension[d] | 16/158 | | 10.1 | 13/156 | | 8.3 | 17/164 | | 10.4 |
| Treatment-emergent parkinsonism (SAS rating)[e] | 1/158 | | 0.6 | 0/157 | | 0 | 7/165 | | 4.2 |
| Treatment-emergent akathisia (BARS rating)[f] | 7/158 | | 4.4 | 14/157 | | 8.9 | 21/165 | | 12.7 |
| Treatment-emergent mania (YMRS rating)[g] | 2/157 | | 1.3 | 1/153 | | 0.7 | 0/164 | | 0 |

HDL=high-density lipoprotein; LDL=low-density lipoprotein; BARS=Barnes Akathisia Rating Scale; SAS=Simpson-Angus Scale; YMRS=Young Mania Rating Scale.

[a]LDL direct and LDL calculated are combined; [b]value recorded in supine position; [c]n/N1=number of patients who met criteria during double-blind treatment / total number of patients with ≥1 postbaseline assessment of interest; [d]≥20 mmHg reduction in systolic blood pressure or ≥10 mmHg reduction in diastolic blood pressure after changing from supine to standing position, [e]SAS ≤3 at baseline and >3 postbaseline; [f]BARS ≤2 at baseline and >2 postbaseline; [g]YMRS total score ≥16 or greater at any visit.

**FIGURE S1.** CONSORT flow diagram for study participants




AE=adverse event; Inc/Exc criteria= patient did not meet inclusion/exclusion criteria; LTF=lost to follow-up; LOE=lack of efficacy; NC=noncompliance with study drug; PV=protocol violation; WOC=withdrawal of consent.