

156 The Broad Efficacy of Cariprazine Across Symptoms in Patients with Bipolar I Disorder: Post Hoc Analysis of Randomized, Placebo-Controlled Trials

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ABSTRACT: Study Objective: Patients with bipolar disorder experience a wide range of depressive and manic symptoms. Only 2 drugs are FDA-approved to treat episodes of both mania and depression in patients with bipolar disorder, highlighting the need for treatments with proven efficacy at opposite poles of the bipolar spectrum. Cariprazine, a dopamine D3-preferring D3/D2 receptor partial agonist and serotonin 5-HT1A receptor partial agonist, is approved in the US for the treatment of both bipolar depression and manic and mixed episodes associated with bipolar I disorder. Cariprazine has previously demonstrated broad efficacy in patients with bipolar mania, with significantly greater improvement in favor of cariprazine vs placebo (PBO) across all individual symptom domains ($P < .001$) measured by the Young Mania Rating Scale (YMRS). Additionally, cariprazine has demonstrated efficacy vs PBO in 3 phase II/III clinical studies in patients with depressive episodes associated with bipolar I disorder (NCT01396447, NCT02670538, NCT02670551). To further assess the broad efficacy of cariprazine in patients with bipolar I disorder, we performed post hoc analyses to evaluate the range of depressive symptoms comprising the individual items of the Montgomery-Åsberg Depression Rating Scale (MADRS) in patients from the bipolar depression studies.

METHODS: Data from the 3 randomized, double-blind, PBO-controlled trials in patients with bipolar depression were pooled. Least squares (LS) mean change from baseline to week 6 in MADRS individual items was assessed in the pooled cariprazine 1.5 and 3 mg/d groups vs PBO using a mixed-effects model for repeated measures in the intent-to-treat (ITT) population.

RESULTS: There were 1383 patients in the ITT population (placebo=460; cariprazine 1.5-3 mg/d=923). At week 6, LS mean change from baseline was significantly greater for cariprazine 1.5-3 mg/d vs PBO on 9 of 10 individual MADRS items: Apparent Sadness (-2.0 vs -1.6, $P < .0001$); Reported Sadness (-2.0 vs -1.6, $P < .0001$); Reduced Sleep (-1.6 vs -1.4, $P = .0357$); Reduced Appetite (-1.2 vs -1.0, $P = .0001$); Concentration Difficulties (-1.5 vs -1.2, $P = .0002$); Lassitude (-1.7 vs -1.4, $P = .0003$); Inability To Feel (-1.7 vs -1.5, $P = .0009$); Pessimistic Thoughts (-1.4 vs -1.2, $P = .0054$) and Suicidal Thoughts (-0.3 vs -0.2, $P = .0383$); differences between cariprazine and PBO on the Inner Tension item were not significant.

CONCLUSIONS: Significant improvement in most MADRS single items suggests broad efficacy in depressive symptoms for cariprazine 1.5-3 mg/d vs PBO in patients with bipolar depression. Coupled with broad efficacy in manic symptoms as demonstrated by significant improvement in all YMRS individual items in patients with bipolar mania or mixed episodes, cariprazine appears to be effective across the range of symptoms that affect patients with bipolar disorder.

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157 Systematic Review: An Educational Strategy to Improve Medication Compliance and Decrease Hospital Readmission Among Adolescents with Bipolar Disorder

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ABSTRACT: The existence of bipolar disorder (BD) among teenagers is controversial. The study aims to review a number of studies regarding the diagnosis of BD in children and teenagers. The prevalence of BD-I is similar throughout many countries, apart from subsyndromal BD, with an estimated 1-3% of teenagers suffering from this illness. Both the presence of subsyndrome BD and full BD have a strong link with psychological difficulties and high risk for use of substances, issues related to legal utilization of services, and suicidality. Diagnosing BD in teenagers is difficult. Therefore, it requires a critical understanding of development stages, evaluation, and accurate recognition and diagnosis. If treatments are delayed, poor outcomes can result. Eight studies were conducted to evaluate the results, based on practices of increasing medical compliance and minimizing hospital

readmission among youths with BD. Randomized trial of family-focused therapy was used to determine early interventions for symptomatic teenagers at risk for BD.

Keywords: interventions, adolescents, compliance, bipolar, decrease in hospitalization

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Open-label Study of Pimavanserin Patients with Comorbid Parkinson's Disease and Depression

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ABSTRACT: Study Objectives: Depression occurs in ~50% of Parkinson's disease (PD) patients, increases in severity and duration as the disease progresses, and is associated with increased morbidity. Improvement of depression in PD patients is correlated with reduced physical disability and improved quality of life. We are assessing use of pimavanserin (PIM) for treatment of depression in adults with PD.

METHOD: A Phase-2, 8-week, open-label, single-arm study is being conducted to evaluate the safety and efficacy of PIM as an adjunct to SSRI/SNRI or as monotherapy in adults with both PD and symptoms of depression (baseline Hamilton Depression Scale [17-items] total score [HAMD-17] ≥ 15). The primary endpoint of the study is change from Baseline to Week 8 in the HAMD-17. Secondary measures included the Clinical Global Impression (CGI) scales (improvement and severity) and Scales of Outcomes in PD-Sleep (SCOPA).

RESULTS: Interim results based on the first 34 of 40 planned patients have been evaluated: 55.9% of patients were male, and average age was 68.1 years, with 19 patients on adjunctive therapy and 15 on monotherapy. At baseline, patients had a mean (SE) HAMD-17 of 19.8(0.6). Change from Baseline to Week 8 (least squares

mean [LSM] [SE]) in the HAMD-17 was -10.7(1.0) (95% CI; -12.7,-8.7; $P < 0.001$), with significant improvement seen as early as Week 2 (-8.4[1.0]; 95% CI; -10.5,-6.4; $P < 0.001$). Significant improvement was seen for both adjunctive treatment and monotherapy: 45.2% of patients responded to treatment ($\geq 50\%$ improvement on the HAMD-17) at Week 8, and 35.5% reached remission (HAMD-17 ≤ 7). On the Clinical Global Impressions-Improvement scale, 54.8% were much/very much improved at Week 8. Significant improvement was seen in change from Baseline to Week 8 SCOPA-Global Sleep Quality, -Nighttime Sleep, and -Daytime Sleepiness: -1.0(0.4) (95% CI; -1.7,-0.3; $P = 0.010$), -2.1(0.7) (95% CI; -3.6,-0.6; $P = 0.008$), -2.1(0.4) (95% CI; -3.0,-1.2; $P < 0.001$) respectively. Twenty-one of the 34 enrolled patients have completed the study to date, and another 7 are still continuing. Thirteen patients reported adverse events, the most common being falls, UTI, diarrhea, and nausea.

CONCLUSIONS: These interim data suggest that PIM as adjunctive treatment or monotherapy is associated with early improvement of depressive symptoms in patients with PD and is well tolerated. This is consistent with recently reported data of PIM in major depressive disorder. Final data will be shared at the time of this presentation. However, additional placebo-controlled data will be needed to determine fully the efficacy of PIM in patients with comorbid PD and depression.
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Safety and Efficacy of Lurasidone in Children and Adolescents with Bipolar Depression: Results from a 2-Year Open-label Extension Study

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ABSTRACT: Background: Bipolar I disorder frequently has an early onset, with an estimated prevalence rate of 1.8% in pediatric populations. Early onset is associated with a high degree of chronicity; however, limited data are available on the long-term efficacy of drug therapies in pediatric populations. The aim of the current study was to evaluate the long-term safety and efficacy of lurasidone in children and adolescents with bipolar depression.