MetSy elevates the risk of developing type II diabetes, cardiovascular disease, and premature morbidity. Lumateperone (LUMA), a mechanistically novel antipsychotic that simultaneously modulates serotonin, dopamine, and glutamate neurotransmission, is FDA-approved for the treatment of schizophrenia and depressive episodes associated with bipolar I or bipolar II disorder. This distinct pharmacological profile has been associated with favorable tolerability and a low risk of adverse metabolic effects in clinical trials.

LUMA 42-mg monotherapy was evaluated in 2 randomized, double-blind, placebo (PBO)-controlled studies (Study 401 [NCT02600494]; Study 404 [NCT03249376]) in patients with a major depressive episode (MDE) associated with bipolar I or bipolar II disorder. This post hoc pooled analysis of these studies compares rates of MetSy with LUMA 42 mg and PBO in the treatment of bipolar depression.

Methods. The incidence and shift in MetSy were analyzed in data pooled from 2 studies that recruited patients aged 18–75 years with a confirmed diagnosis of bipolar I or bipolar II disorder who were experiencing an MDE (Montgomery-Åsberg Depression Rating Scale [MADRS] Total score ≥20 and Clinical Global Impression Scale-Bipolar Version-Severity [CGI-BP-S] score ≥4). Patients in these studies were randomized 1:1 to LUMA or PBO and treated for 6 weeks.

Results. The safety population comprised 746 patients (LUMA, 372; PBO, 374). Rates of MetSy were similar between groups at baseline (LUMA, 20.7%; PBO, 22.2%) and at the end of treatment (EOT, LUMA, 21.8%; PBO, 23.8%). More LUMA patients (36.4%) compared with PBO patients (30.1%) improved from having MetSy at baseline to no longer meeting MetSy criteria at EOT. The individual criteria that shifted the most from meeting MetSy criteria at baseline to no longer meeting criteria at EOT was BP for LUMA (46.8%) and glucose for PBO (43.2%). The rate of MetSy developed during treatment was similar for LUMA (10.8%) and PBO (10.7%) with approximately half of these patients (LUMA, 43.8%; PBO, 45.2%) shifting due to a change in ≥2 criteria.

Conclusion. In this post hoc analysis of 2 randomized, PBO-controlled trials in patients with a MDE associated with bipolar I or bipolar II disorder, LUMA 42 mg had similar rates of MetSy compared with PBO. These results suggest that LUMA 42 mg is a promising new treatment for bipolar depression with a favorable metabolic profile.

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Efficacy and Safety of Lurasidone in a Younger Population With Bipolar Depression: Pooled Post-hoc Analysis of Two Placebo-controlled Studies

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Abstract

Introduction. Early onset of bipolar disorder is associated with high rates of psychiatric comorbidity (e.g., anxiety disorders, ADHD, PTSD), high rates of recurrence, and marked impairment in functioning and quality of life. The aim of this analysis was to evaluate the efficacy and safety of lurasidone in bipolar depression in youth and young adult patients (10–30 years old).

Methods. Data from two 6-week, double-blind, placebo-controlled studies of lurasidone monotherapy for bipolar I depression were pooled for this analysis. In the 1st study, patients 10–17 years old were evaluated using the Children's Depression Rating Scale–Revised (CDRS-R) and the Clinical Global Impression-Bipolar Severity (CGI-BP-S) depression scale; in the 2nd study, a subgroup of adult patients (18–30 years old) were evaluated by CGI-BP-A, and the MADRS, with the latter being converted to a CDRS-R scores using a validated conversion algorithm.

Results. The safety population consisted of 465 patients (mean age, 17.1 years; mean age of onset, 14.1; mean CDRS-R total score, 60.8). 400 patients (85.7%) completed the study. For lurasidone vs. placebo, LS mean Week 6 change was -21.4 vs. -15.3 for the CDRS-R total score (P<0.0001; ES, 0.46); and -1.6 vs. -1.1 for the CGI-BP-S score (P<0.0001; ES, 0.50). Adverse events (≥5%) on lurasidone vs. placebo were nausea (15.9% vs. 5.2%), headache (15.1% vs. 13.1%), somnolence (7.9% vs. 3.8%), vomiting (5.2% vs. 3.3%), and weight increase (5.2% vs. 2.3%). No clinically meaningful changes were observed in weight, metabolic parameters, or prolactin.

Conclusions. In this post-hoc analysis of two placebo-controlled trials, lurasidone demonstrated clinically meaningful improvement of depressive symptoms in youth and young adults with bipolar depression. Lurasidone was generally safe, well-tolerated, and associated with minimal effects on weight, metabolic parameters, and prolactin.

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Long-Term Safety and Effectiveness of Lurasidone in Adolescents and Young Adults With Schizophrenia: Pooled Post-hoc Analyses of Two 12-month Extension Studies

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