

Efficacy of Lurasidone in Patients With Schizophrenia With Prominent Positive Symptoms: A Pooled Analysis of Short-Term, Placebo-Controlled Studies

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Abstract

Background: Acute schizophrenia is characterized by the presence of active positive symptoms, which may be disruptive to the patient and increase the risk of behavioral disturbance and hospitalization. This pooled, post hoc analysis evaluated the efficacy of lurasidone in patients with acute schizophrenia with prominent positive symptoms. **Methods:** Patient-level data were pooled from five similarly designed, multiregional, randomized, double-blind, placebo-controlled, six-week studies of fixed-dose lurasidone (40, 80, 120 or 160mg/d) conducted in adult patients (age 18–75) with acute schizophrenia. Prominent positive symptoms were defined as baseline Positive and Negative Syndrome Scale (PANSS) positive subscale score greater than baseline PANSS negative subscale score. Treatment response was defined as at least a 30% decrease in PANSS total score at week 6 (last observation carried forward [LOCF]).

Results: This analysis included 919 patients with prominent positive symptoms (mean age=38.5, 72.3% male) and 613 patients without prominent positive symptoms (mean age=38.3, 74.1% male). Study discontinuation rates were 39.5% for lurasidone and 48.7% for placebo in patients with prominent positive symptoms and 29.5% for lurasidone and 36.2% for placebo in patients without prominent positive symptoms. Based on change from baseline to week 6 in PANSS total score (mixed-model repeated-measures analysis), effect sizes for the lurasidone 40, 80, 120 and 160mg/d dose groups were 0.51, 0.65, 0.44 and 1.09, respectively, for patients with prominent positive symptoms (all $p < 0.001$) and 0.29, 0.46, 0.55 and 0.67, respectively, for patients without prominent positive symptoms ($p < 0.05$ for 40mg/d, all other $p < 0.001$). In patients with prominent positive symptoms, treatment response (at least 30% improvement in PANSS total score) at week 6 LOCF was observed in 29.3% of patients in the placebo group and 48.3%, 46.6%, 43.2% and 64.4% of patients in the lurasidone 40, 80, 120 and 160mg/d dose groups, respectively (with associated number needed to treat [NNT] of 6, 6, 8 and 3, respectively). In patients without prominent positive symptoms, treatment response at week 6 LOCF was observed in 35.7% of patients in the placebo group and 50.0%, 52.1%, 54.5% and 60.4% of patients in the lurasidone 40, 80, 120 and 160mg/d dose groups, respectively (NNT of 7, 7, 6 and 5, respectively).

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Conclusion: In adult patients with schizophrenia presenting with prominent positive symptoms, lurasidone therapy was associated with medium to large treatment effects sizes. Larger effect sizes were observed in patients with prominent positive symptoms compared to patients without prominent positive symptoms. These results may inform the design of future clinical trials in schizophrenia. This study was supported by Sunovion Pharmaceuticals, Inc.

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