Efficacy of Lurasidone in Antipsychotic-Naive vs. Antipsychotic-Exposed Adolescents with Schizophrenia: Post-Hoc Analysis of a Two-Year, Open-Label Study

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Abstract

Background. Few studies have examined treatment response in adolescents with schizophrenia who are treatment-naive; and there is no placebo-controlled study that we are aware of in first episode treatment-naive patients with schizophrenia. The aim of this analysis was to evaluate the long-term efficacy of lurasidone in antipsychotic-naive adolescents with schizophrenia.

Method. Patients aged 13–17 years with schizophrenia, and a PANSS total score ≥70 and <120, were randomized to 6 weeks of double-blind (DB) treatment with lurasidone (40 or 80 mg/day) or placebo. Six-week completers were eligible to enroll in a 2-year open-label extension phase receiving lurasidone flexibly dosed from 20–80 mg/day. In a post-hoc analysis, efficacy was evaluated for 2 patient groups based on treatment status prior to entering the initial 6-week DB study (treatment naïve [TN] vs. treated previously [TP]). Treatment-naïve was defined as never having received antipsychotic treatment. Efficacy measures included the PANSS total score and the Clinical Global Impression, Severity (CGI-S) score. Level of functioning was assessed using the Children's Global Assessment Scale (CGAS), with a score of 70 representing normative levels of functioning.

Results. A total of 50 TN and 221 TP patients completed the 6-week DB study and entered the extension study; and 30 (60.0%) TN and 126 (57.0%) TP patients completed 104 weeks. During the initial 6 weeks of DB treatment, mean change in PANSS total score at endpoint was greater for lurasidone vs. placebo in both the TN group (−25.0 vs. −14.4; P<0.02; effect size, 0.75), and in the TP group (−17.3 vs. −10.0; P<0.001; effect size, 0.45). During OL extension phase treatment with lurasidone, mean change from DB baseline in the PANSS total score for TN and TP patients, at week 52 was −32.6 (n=38) and −28.1 (n=151), respectively; and at week 104 was −33.6 (n=30) and −29.2 (n=126), respectively. Mean change from DB baseline in CGI-S score at both weeks 52 and 104 was −1.8 for TN patients and −1.5 for TP patients. At DB baseline mean CGAS scores indicated significant functional impairment in both the TN and TP patients (CGAS=48 and 43, respectively). During OL treatment with lurasidone, mean change (from DB baseline) in the CGAS score at Weeks 52 and 104, respectively, was +22.0 and +22.9 in TN patients, and +21.1 and +22.9 in TP patients. During OL treatment with lurasidone, mean observed change from DB baseline in the weight (in kg,) at Weeks 52 and 104, respectively, was +4.2 and +4.8 in TN patients, and +4.0 and +5.0 in TP patients. These weight increases are consistent with expected weight gains in adolescents during a 2-year period (based on CDC growth charts).

Conclusions. In this post-hoc analysis of a 2-year study, adolescents with schizophrenia who had received no previous antipsychotic therapy showed greater improvement compared to previously treated patients during both short- and long-term treatment with lurasidone.

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Effect of Lurasidone on Manic Symptoms and Treatment-Emergent Mania in Adult and Pediatric Populations with Bipolar Depression

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Abstract

Background. Lurasidone is approved for the treatment of bipolar depression both as monotherapy and adjunctive therapy with lithium or valproate (Li/VPA). The aim of these analyses was to evaluate the prevalence of treatment-emergent mania (TEM) and worsening of mania symptom severity in clinical trials of both adult and pediatric patients with bipolar depression treated with lurasidone.

Method. In these post-hoc analyses, TEM and change in manic symptom severity as measured by the Young Mania Rating Scale (YMRS) were evaluated in two double-blind (DB), 6-week studies in adults of lurasidone monotherapy, 20–60 mg/d (n=161) and 80–120 mg/d (n=162) vs. placebo (n=162), and adjunctive therapy of lurasidone 20–120 mg/d + Li/VPA (n=179) vs. placebo + Li/VPA (n=161). Prevalence of TEM was also evaluated in a 6-month, open-label (OL) extension study of adults treated with lurasidone monotherapy (n=316) or adjunctive therapy (n=497). In pediatric patients (ages 10–17) TEM and change in manic symptoms was evaluated in a DB 6-week study of lurasidone monotherapy (n=173) vs. placebo (n=170) and in a 24-month OL extension study. TEM was defined as an adverse event of mania or hypomania and/or having a YMRS score =16 at 2 consecutive post-baseline weekly visits (or the final assessment) in short-term studies or 1 post-baseline monthly visit in long-term studies.

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