

EFFECT OF LURASIDONE ON MANIC SYMPTOMS AND TREATMENT-EMERGENT MANIA IN CHILDREN AND ADOLESCENTS WITH BIPOLAR DEPRESSION

Michael Tocco, PhD; Andrei Pikalov, MD, PhD; Courtney Zeni, PhD; Robert Goldman, PhD
Sunovion Pharmaceuticals Inc, Marlborough MA

ABSTRACT

Background: The aim of these analyses was to assess the effect of lurasidone on manic symptoms and treatment-emergent (TE) mania in pediatric patients with bipolar depression.
Methods: Patients (ages 10-17) were randomized, double-blind (DB) to 6-weeks of lurasidone 20-80 mg/d (n=173) or placebo (n=170). Study completers were eligible to enter a 24-month open-label (OL) extension study of lurasidone (20-80 mg/day). Manic symptoms were measured using the Young Mania Rating Scale (YMRS). TE-mania was defined as an adverse event of mania/hypomania or having a YMRS score ≥ 16 at 2 consecutive post-baseline weekly visits in short-term studies, or 1 post-baseline monthly visit in the OL extension.
Results: 305 patients entered the extension study; 195 and 93 completed 52 and 104 weeks of treatment, respectively. TE-mania rates were comparable in pediatric patients treated with lurasidone vs. placebo (1.7% vs. 2.3%). LS mean reduction in symptoms of mania from baseline to week 6 was significantly greater for lurasidone vs. placebo on YMRS score (-2.0 vs. -1.1; $p < 0.05$). After two years of open-label treatment with lurasidone, 5.2% of patients met TE-mania criteria. Mean change in YMRS total score from double-blind baseline to Month 24 continued to improve (-2.0).
Conclusion: During 6 weeks of treatment, TE-mania rates were comparable for both lurasidone and placebo groups. Over 2 years of lurasidone therapy, TE-mania was only observed in a small proportion of patients. Both short- and long-term treatment with lurasidone demonstrated improvement in manic symptoms in this patient population.

INTRODUCTION

- Bipolar I disorder is a chronic, recurrent illness, with an onset prior to adulthood in approximately 25% of individuals. In most patients, depression is the first episode experienced, either with symptoms similar to unipolar depression (50% of patients), or with mixed depressive and manic symptoms (28%; Suppes et al, J Affec Disord 2001;67:45-59)
- Longitudinal assessment indicates that the majority of time in an affective episode is spent in a depressed state (68%), followed by mania or hypomania (20%), and a mixed state or rapid cycling (12%; Judd et al, Arch Gen Psych 2002;59:530-37)
- Antidepressants are a commonly used and frequently effective treatment of bipolar depression; however, they can trigger a switch from depression to mania, especially tricyclic antidepressants
- Lurasidone is approved for the treatment of bipolar depression both as monotherapy and adjunctive therapy with lithium or valproate (Li/VPA). Lurasidone has also demonstrated efficacy in the treatment of MDD with mixed features, a diagnosis new to DSM-5 that has been estimated to comprise more than one-third of all cases of MDD

OBJECTIVE

- The aim of these analyses is to assess the effect of lurasidone on treatment-emergent mania, and manic symptoms and severity, in both adult and pediatric patients with bipolar depression

METHODS

- In these secondary analyses of patients with a diagnosis of bipolar I depression, treatment-emergent mania, manic symptoms, and severity of mania, as measured by the Young Mania Rating Scale (YMRS) or the Clinical Global Impression Bipolar Severity (CGI-BP-S) mania score, were evaluated in the following **short-term lurasidone studies in adults:** (1) **monotherapy:** 1 double-blind, 6-week studies of lurasidone, 20-60 mg/d (n=161) and 80-120 mg/d (n=162) vs. placebo (n=162); (2) **adjunctive therapy:** 1 double-blind, 6-week study of lurasidone 20-120 mg/d + Li/VPA (n=179) vs. placebo + Li/VPA (n=161); and **long-term studies in adults:** (1) a 6-month, open-label extension study of patients treated with lurasidone **monotherapy** (n=316) or **adjunctive therapy** (n=497). Treatment-emergent mania and manic symptoms were also evaluated in a study of patients with major depressive disorder (MDD) with mixed features, a diagnosis that is new to DSM-5, and may represent more than 25% of all cases of MDD
- Treatment-emergent mania and manic symptom severity, were also evaluated in the following **monotherapy studies of pediatric patients** (ages 10-17): (1) a double-blind, 6-week study of lurasidone (n=173) vs. placebo (n=170); and (2) a 24-month open-label extension study of lurasidone (n=305)
- Treatment-emergent mania was defined as an adverse event of mania or hypomania or having a YMRS score ≥ 16 at 2 consecutive post-baseline visits (or the final assessment) in short-term studies or 1 post-baseline visit in long-term studies

RESULTS

Figure 1. Effect of Short-term Treatment with Lurasidone (Monotherapy and Adjunctive Therapy) on the YMRS Score and on Rates of Treatment-emergent Mania: Adults with Bipolar Depression

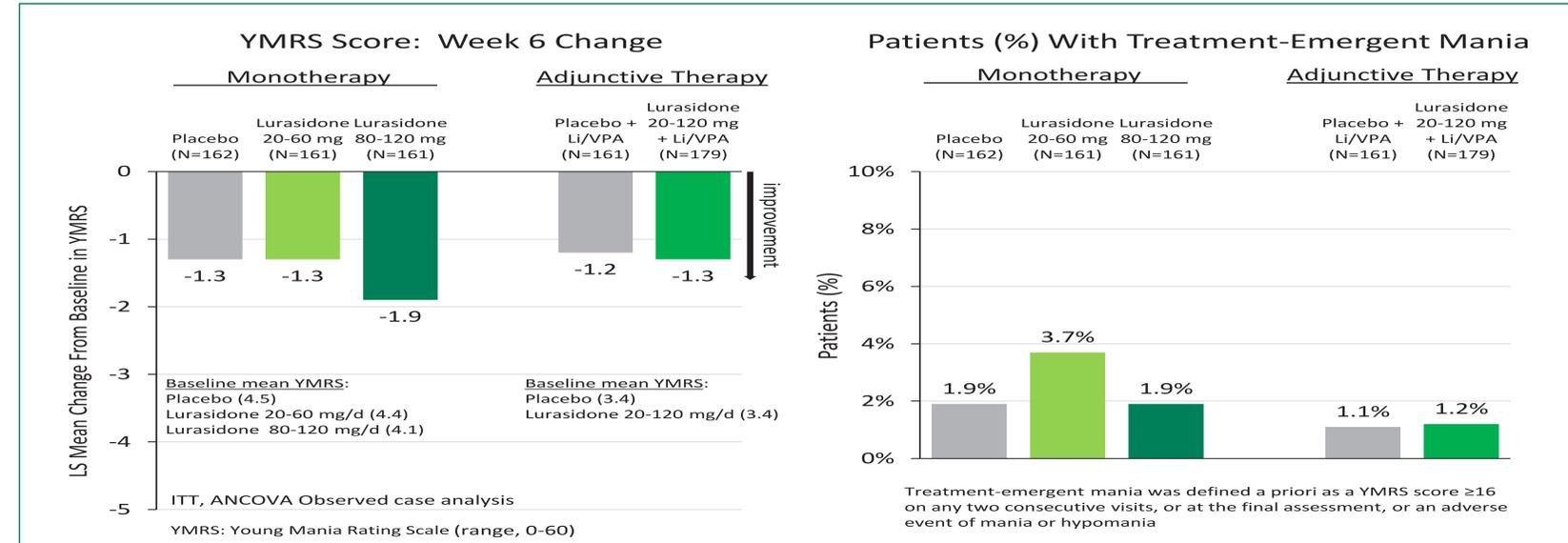


Figure 2. Effect of Short-term Monotherapy with Lurasidone on the YMRS Total and Item Scores, and on Rate of Treatment-emergent Mania: Adults with MDD with Mixed Features

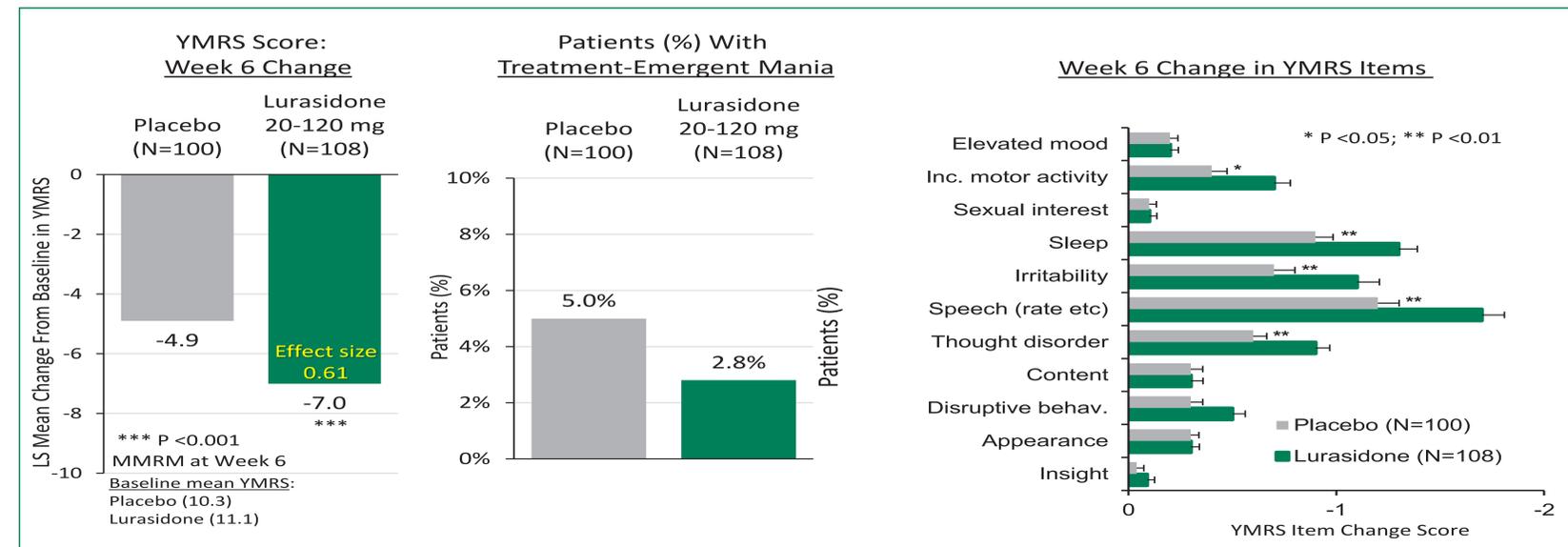


Figure 3. Effect of Short-term Monotherapy with Lurasidone on the YMRS and CGI-BP-S Mania Scores, and on Rates of Treatment-emergent Mania: Pediatric Patients with Bipolar Depression

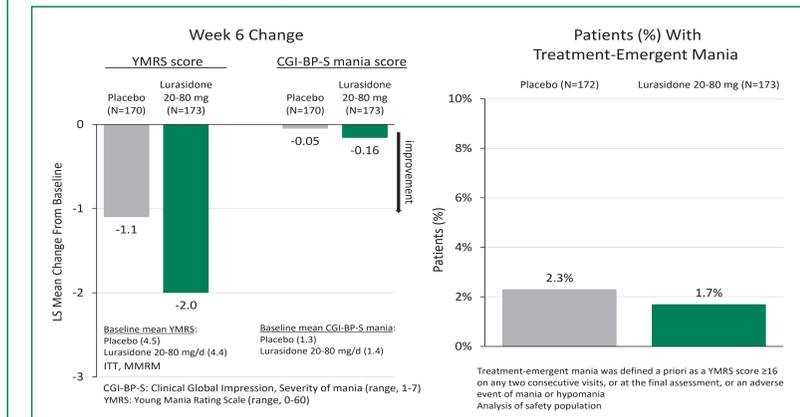


Figure 4. Treatment-emergent Mania During Long-term Treatment with Lurasidone: Adults

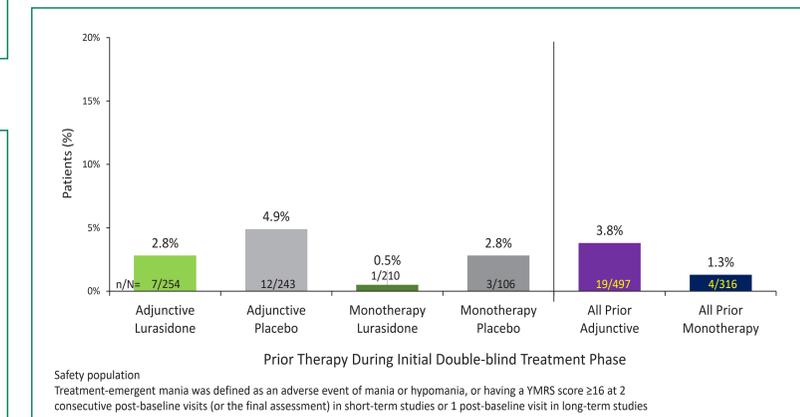
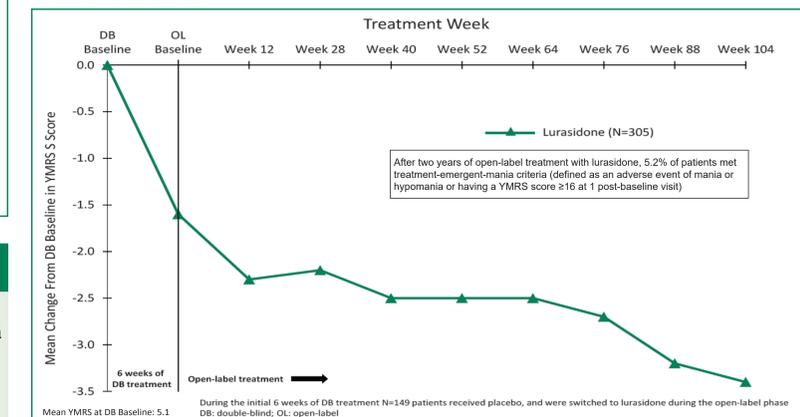


Figure 5. Change in YMRS Score During Long-term Treatment with Lurasidone: Pediatric Patients



DISCLOSURES

Dr. Tocco, Pikalov, Zeni and Goldman are employees of Sunovion Pharmaceuticals Inc. Dr. Edward Schweizer, of Paladin Consulting Group, provided editorial and medical writing assistance, which was funded by Sunovion Pharmaceuticals Inc.

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DISCUSSION

- Short and long-term treatment with lurasidone in adults and children with bipolar depression was associated with improvement of manic symptoms and no increased rate of treatment emergent mania relative to placebo
- Similar effects on mania were observed in adult patients with MDD with mixed features treated with lurasidone