LONG-TERM EFFICACY OF LURASIDONE IN PEDIATRIC BIPOLAR DEPRESSION: POST-HOC ANALYSIS OF RESPONSE, REMISSION AND RECOVERY

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INTRODUCTION and OBJECTIVE

- Bipolar disorder frequently has an early onset, with an estimated 1.8% prevalence rate of bipolar I disorder in pediatric populations
- Childhood onset of bipolar disorder is frequently associated with a more chronic and severe course of illness compared with patients with an onset in adulthood, including impairment in functioning and quality of life
- Lurasidone is approved by the FDA for the treatment of bipolar depression in adults as monotherapy, and as adjunctive therapy with lithium or valproate
- Lurasidone has demonstrated efficacy in the treatment of children and adolescents with bipolar depression, and has been approved by the FDA as monotherapy for bipolar depression in pediatric patients ages 10-17 years
- The aim of this secondary analysis was to evaluate the long-term efficacy of lurasidone in achieving response, remission and recovery in children and adolescents with bipolar depression

METHODS

- Patients 10-17 years with bipolar I depression who completed a 6-week double-blind (DB) study of lurasidone vs. placebo were eligible to enroll in a 2-year, open-label (OL) extension study in which patients were continued on flexibly-dosed lurasidone (20-80 mg/d) or switched from placebo to lurasidone
- Efficacy measures included the Children's Depression Rating Scale, Revised (CDRS-R) and the Clinical Global Impression, Bipolar Depression Severity scale (CGI-BP-S). Functioning was evaluated utilizing the Clinician-rated Children's Global Assessment Scale (CGAS) score, with a score ≥70 indicating no clinically meaningful functional impairment
- **Responder criteria:** ≥50% reduction from DB baseline in the CDRS-R total score. **Remission criteria:** a CDRS-R Total Score ≤28, a YMRS total score ≤8, and a CGI-BP-S depression score ≤3. **Recovery criteria:** patient meets remission criteria and has a CGAS score ≥70. **Sustained remission criteria:** patient meets remission criteria for ≥24 consecutive weeks

RESULTS

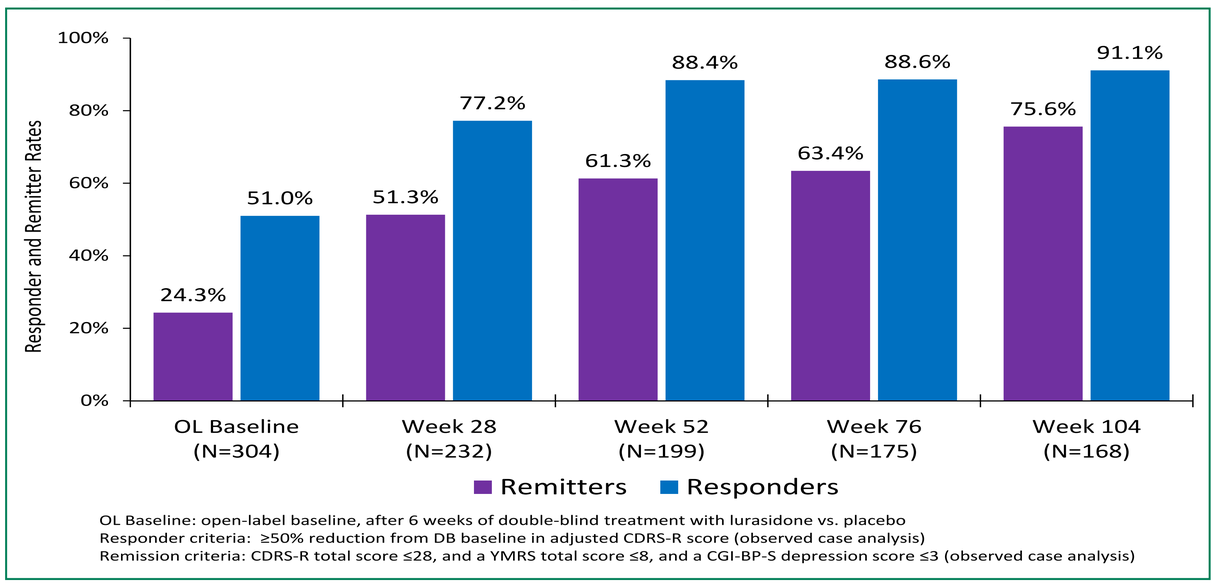
Table 1. Patient Characteristics, Open-label Baseline

Characteristic	Lurasidone to Lurasidone (N=156)	Placebo to Lurasidone (N=149)
Male, %	50.0	50.3
Age, years, mean	14.4	14.5
Race, %		
White	77.6	76.5
Black/African-American	7.7	9.4
Other	14.7	14.1
Baseline Scores, Double-blind/Open-label		
CDRS-R Total Score	59.4 / 36.6	58.7 / 41.9
CGI-BP-S Depression Score	4.57 / 3.04	4.46 / 3.42

CDRS-R = Childhood Depression Rating Scale-Revised; CGI-BP-S = Clinical Global Impression-Bipolar-Severity;

- The mean dose of lurasidone averaged over the open-label treatment period was 54.5 mg/d; and the modal dose was 20 mg (6.6% of patients), 40 mg (41.6%), 60 mg (25.9%), and 80 mg (25.9%)
- Of the 306 patients who entered the extension study 168 (54.9%) completed 2 years of OL treatment. Reasons for discontinuation consisted of withdrawal of consent (15.4%), adverse event (10.1%), lost to follow-up (6.2%), protocol violation (6.2%), lack of efficacy (1.6%) and other reasons (5.2%)

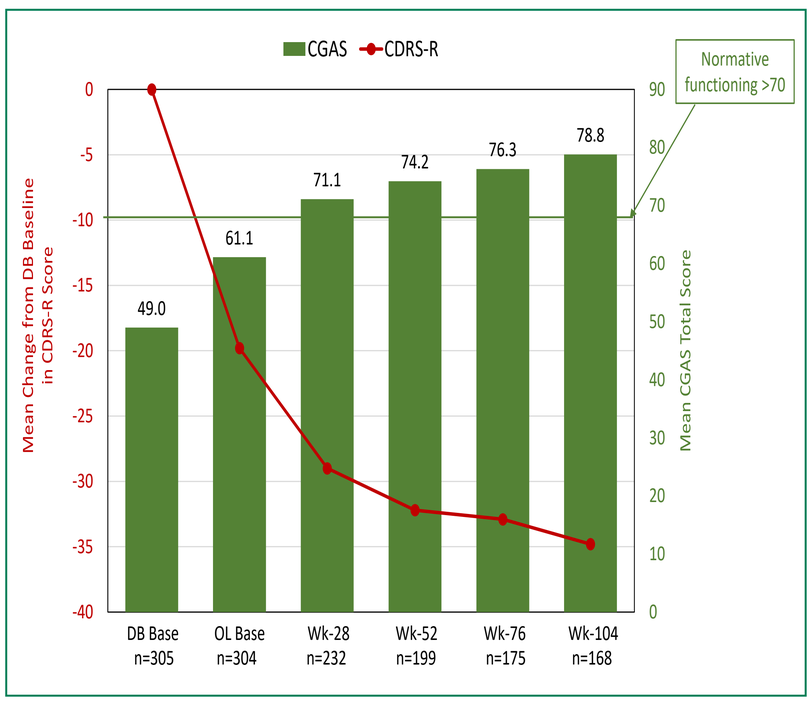
Figure 1. Responder & Remitter Rates During Open-label Treatment with Lurasidone



OL Baseline: open-label baseline, after 6 weeks of double-blind treatment with lurasidone vs. placebo
Responder criteria: ≥50% reduction from DB baseline in adjusted CDRS-R score (observed case analysis)
Remission criteria: CDRS-R total score ≤28, and a YMRS total score ≤8, and a CGI-BP-S depression score ≤3 (observed case analysis)

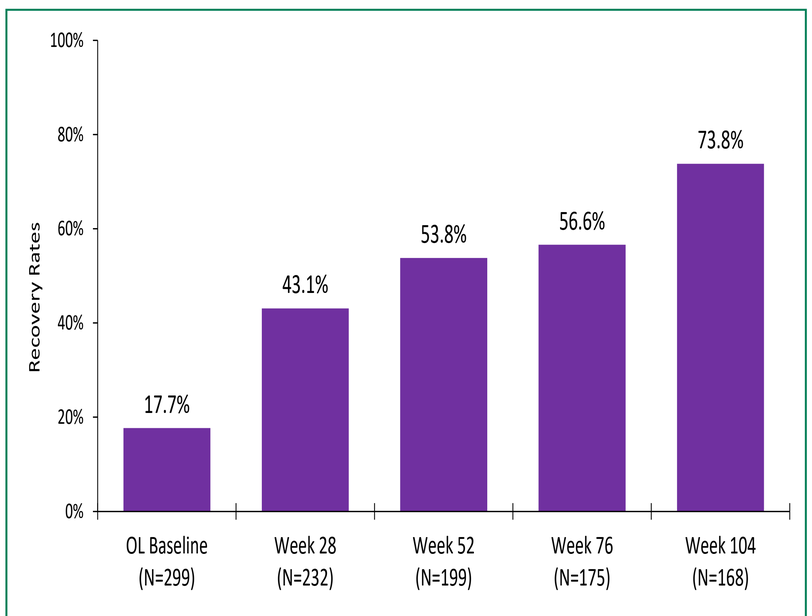
- A Kaplan-Meier analysis found a longer time-to-remission in patients who were treated with placebo for 6 weeks during the initial double-blind phase (prior to switching to lurasidone) compared to patients treated with lurasidone from the beginning of the double-blind phase (median [95%-CI]: 85 [43, 99] days vs. 197 [85-197] days
- In this adolescent population, it appears that delaying onset of active treatment by 6 weeks may be associated with a lag in the median time to remission. If confirmed by future studies, this suggests that early recognition of the onset of a depressive episode, and early treatment intervention, may be important for achieving remission

Figure 2. Change From Baseline in CDRS-R Score, and Mean CGAS Total Score During Open-label Treatment With Lurasidone



- A Pearson correlation analysis found a significant inverse correlation between reduction in the CDRS-R score and improvement in functioning as measured by the CGAS total score (r = -0.71; P <0.0001)

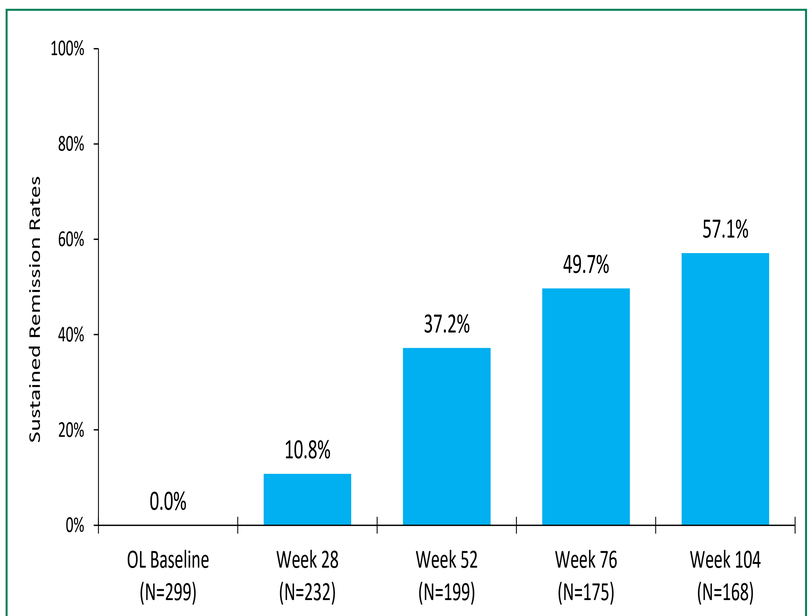
Figure 3. Recovery Rates During Open-label Treatment with Lurasidone



Recovery was defined as meeting remission criteria (CDRS-R Total Score ≤28, a YMRS total score ≤8, and a CGI-BP-S depression score ≤3), plus meeting one additional criterion: CGAS score ≥70

- The proportion of patients who met criteria for treatment-emergent mania or hypomania at any time during 2-years of open-label treatment was 5.2% (based on YMRS total score ≥15 for 2 consecutive visits, or at 1 visit if it was the final study visit)

Figure 4. Sustained Remission During Open-label Treatment with Lurasidone



Sustained remission was defined as meeting remission criteria for ≥24 consecutive weeks (includes patients who initially met remission criteria during the double-blind treatment phase)

DISCLOSURES

Dr. Singh has received research support from Stanford's Maternal Child Health Research Institute, NIMH, National Institute of Aging, Johnson and Johnson, Allergan, and the Brain and Behavior Research Foundation. She is on the advisory board for Sunovion, is a consultant for GoogleX and Limbix, andreceives royalties from the American Psychiatric Association Publishing. Drs. Tocco and Pikalov are employees of Sunovion Pharmaceuticals Inc. Medical writing support was provided by Edward Schweizer, MD of Paladin Consulting Group, and was funded by Sunovion Pharmaceuticals Inc

Supported by funding from Sunovion Pharmaceuticals Inc.

NNDC Virtual Meeting, September 21-22, 2021

DISCUSSION

- In children and adolescents with bipolar depression, up to 2-years of treatment with lurasidone was associated with continued improvement in depressive symptoms, resulting in progressively higher rates of remission and recovery
- In the current study, the sustained remission rate, which is a proxy for long term clinical stability, provide important data for therapeutic decision making in this difficult to treat and vulnerable population
- In children and adolescents, rates of treatment-emergent mania were very low over the course of two years of lurasidone therapy