

Plain Language Summary



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Lumateperone Treatment of Manic Episodes With or Without Mixed Features in Bipolar I Disorder: Results From a Double-Blind, Placebo-Controlled, Randomized, Phase 3 Trial

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What do the results mean for individuals with Bipolar I disorder?

In a clinical trial, lumateperone 42 mg was evaluated for the treatment of manic episodes with or without mixed features in adult patients with bipolar I disorder. Results showed a statistically significant and clinically meaningful change in Young Mania Rating Scale (YMRS) total score from baseline, starting at Day 3 and up until Day 22, compared with placebo.

What was the purpose of this study?

To understand the efficacy and safety of lumateperone for treatment of manic episodes in adults with bipolar I disorder, including those with mixed features.



- **Lumateperone:** An atypical antipsychotic that has been shown to improve depressive symptoms in adults in clinical trials and has been approved for the treatment of schizophrenia, depressive episodes associated with bipolar I or II disorder, and as adjunctive therapy with antidepressants for major depressive disorder
- **Bipolar I disorder:** A mental health condition in which a person experiences at least one manic episode, which may occur before or after hypomanic and/or major depressive episodes
- **Manic episode:** A period of at least one week of unusually elevated or irritable mood, increased energy, and/or increased activity, which may also involve impulsive behavior
- **Mixed features:** Presence of symptoms of both depression and mania/hypomania at the same time during a mood episode

How was the study conducted and what was the design?

The study was a Phase 3, randomized, double-blind, placebo-controlled trial in which patients were assigned 1:1 to receive either lumateperone 42 mg or placebo once daily for 3 weeks followed by a 1-week safety follow-up. Adult hospitalized patients diagnosed with bipolar I disorder according to DSM-5 criteria, who were experiencing a current manic episode, with or without mixed features, that began ≤ 4 weeks before Visit 1 were included. Patients were required to have a YMRS total score ≥ 20 , with marked symptoms (score ≥ 4) in at least two key areas (irritability, speech, thought content, or disruptive/aggressive behavior) and a Clinical Global Impression–Severity (CGI-S) score ≥ 4 at Visits 1 and 2.



- **YMRS:** A clinical tool used to assess the severity of **manic symptoms**. YMRS is measured on a scale of 0–60, with a score of ≥ 25 indicating severe illness
- **Remission:** YMRS score of ≤ 12
- **CGI-S:** A scale used to measure the severity of **overall mental illness**. CGI-S is measured on a scale of 0–7

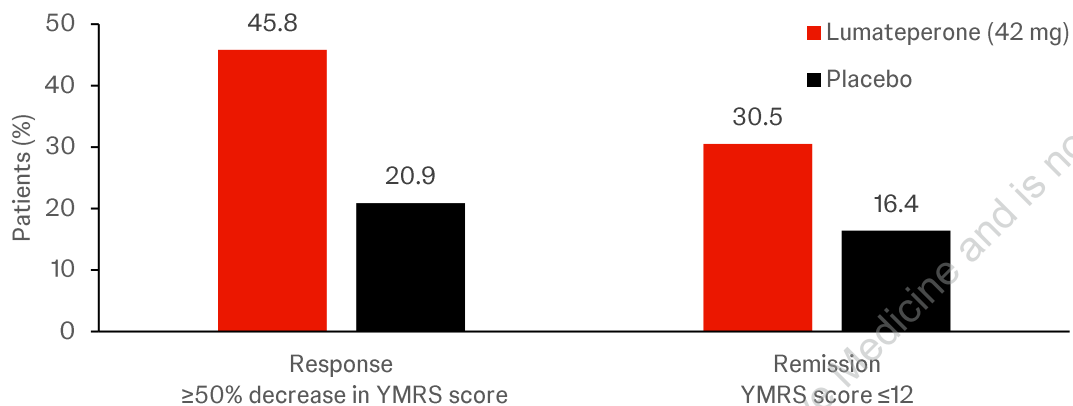
What were the results of the analysis?

There were 177 patients treated with lumateperone and 177 treated with a placebo. The average age of patients was 46.6 years, 58.8% of patients had experienced ≤ 5 manic episodes in their lifetime, and 15.3% of patients had mixed features. YMRS total scores at baseline indicated that most patients were experiencing severe mania (lumateperone group: 33.2; placebo group: 32.1).

Results showed a statistically significant change in YMRS total score from baseline through to Day 22 compared to placebo with a least square mean difference (LSMD) of -4.8 ($p < 0.0001$) and improvements as early as Day 3.

More patients receiving lumateperone showed significantly greater response (YMRS total score $\geq 50\%$ decrease; $p < .0001$) and remission (YMRS total score ≤ 12 ; $p = .0009$) compared with those who received placebo. Statistically significant improvements in CGI-S score were achieved from baseline through to Day 22 compared with placebo, with a LSMD -0.5 ($p < 0.0001$).

Change in YMRS score after 3 weeks of treatment leading to response or remission



Less than 2% of patients in the lumateperone group discontinued treatment due to adverse events.



Common adverse events that occurred during treatment with frequency ≥2% and a higher rate than placebo were:

- Headache
- Dry mouth
- Nausea
- Dizziness
- Somnolence
- Anxiety
- Diarrhea
- Agitation
- Vomiting
- Hyperinsulinemia
- Nasopharyngitis
- Vulvovaginal mycotic infection