

Lumateperone (ITI–007) in the Treatment of Bipolar Depression: Results from a Randomized Clinical Trial

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Abstract

Study Objective. Approved treatments for bipolar depression are limited and associated with a spectrum of undesirable side effects. Lumateperone (lumateperone tosylate, ITI–007), a mechanistically novel antipsychotic that simultaneously modulates serotonin, dopamine, and glutamate neurotransmission, is FDA-approved for the treatment of schizophrenia. Lumateperone is currently being investigated for the treatment of bipolar depression (major depressive episodes [MDE] associated with bipolar I and bipolar II disorder). This Phase 3 randomized, double-blind, parallel-group, placebo-controlled multinational study (NCT03249376) investigated the efficacy and safety of lumateperone in patients with bipolar I or bipolar II disorder experiencing a MDE.

Method. Patients (18–75 years) with a clinical diagnosis of bipolar I or bipolar II disorder who were experiencing a MDE (Montgomery-Åsberg Depression Rating Scale [MADRS] Total score =20 and a Clinical Global Impression Scale-Bipolar Version-Severity [CGI-BP-S] score =4 at screening and baseline) were randomized to lumateperone 42mg or placebo for 6 weeks. The primary and key secondary efficacy endpoints were change from baseline to Day 43 in MADRS total score and CGI-BP-S scores, respectively. Secondary efficacy outcomes included response (MADRS improvement = 50%) and remission (MADRS total score =12) at Day 43. Safety assessments included treatment emergent adverse events, laboratory parameters, vital signs, extrapyramidal symptoms (EPS), and suicidality.

Results. In this study, 377 patients received treatment (placebo, n=189; lumateperone 42mg, n=188) and 333 completed treatment. Patients in the lumateperone 42-mg group had significantly greater mean improvement on MADRS total score change from baseline to Day 43 compared with placebo (least squares mean difference [LSMD]=−4.6; 95% confidence interval [CI]=−6.34, −2.83; effect size vs placebo [ES]=−0.56; P<.0001). Lumateperone treatment was associated with significant MADRS improvement in both patients with bipolar I (LSMD=−4.0; 95% CI=−5.92, −1.99; ES=−0.49; P<.0001) and bipolar II (LSMD=−7.0; 95% CI=−10.92, −3.16; ES=−0.81; P=.0004). The lumateperone 42-mg group also had significantly greater mean improvement in CGI-BP-S total score compared with placebo (LSMD=−0.9; 95% CI=−1.37, −0.51; ES=−0.46; P<.001). Lumateperone compared with placebo had significantly greater MADRS response rate (51.1% vs 36.7%; odds

ratio=2.98; P<.001) and remission rates (P=.02) at Day 43. Lumateperone treatment was well tolerated, with minimal risk of EPS, metabolic, and prolactin side effects.

Conclusions. Lumateperone 42 mg significantly improved depression symptoms in both patients with bipolar I and bipolar II depression. Lumateperone was generally well tolerated. These results suggest that lumateperone 42 mg may be a promising new treatment for bipolar depression associated with bipolar I or bipolar II disorder.

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Evidence Based Approach to Capacity Assessment for Hospitalized Patients

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Abstract

Medical decision-making capacity (MDMC) is inherent to the legal and ethical principles of respect for autonomy and is an essential element of informed consent. Qualitative and quantitative evidence to support a final decision of capacity should be the gold standard. General hospital policies and state laws mandate that a licensed provider make the final determination of capacity, but they do not specifically mandate who is responsible for those assessments. When a patient's decisional capacity fluctuates, the role of the nurse in a hospital setting is valuable because they have the most direct contact with the patient. Objective: Determine receptiveness of nursing staff to assessing capacity, to gather feedback on the Aid to Capacity Evaluation (ACE) tool, and to ascertain awareness of capacity by sixty nurses working on progressive care, trauma orthopedic, and medical/surgical units. Method: This project was completed at a Midwestern academic level I trauma center. Nurses on a medical/surgical, orthopedic trauma, and progressive care unit participated. Education about MDMC and the ACE tool were given to nurses verbally and in writing. They were asked to utilize the Aid to Capacity Evaluation (ACE) tool to assess patients whom they believed lacked decision-making capacity. After four weeks the nurses completed an evaluation. Results: Thirty nurses (50%) responded. Over 70% of those respondents used the tool at least once. 63% agreed that the format helped to systematically evaluate a patient and they found it easy to incorporate into practice. Overall, 73% of respondents would welcome more education about capacity. Conclusion: Given a standardized tool in conjunction with proper and continuous education, bedside nurses are in an optimal position to identify mental changes early, alert the provider so steps can be taken to optimize mental capacity, and assist with assessment of capacity with minimal disruption of care. Implementation of a tool such as the ACE can ensure accurate, reliable, and consistent assessments. Furthermore, providers would benefit from the extra time to gather information and complete focused assessments to make a determination of capacity with confidence.