were evaluated throughout the study; assessments included adverse event reporting, patient reporting of injection site pain, and monitoring of extrapyramidal symptoms.
Results. In the Ari 2MRTU group, 102 patients (77.3%) completed the study; in the AOM 400 group, 92 patients (68.7%) completed the study. The overall incidence of treatment-emergent adverse events (TEAEs) was similar between Ari 2MRTU 960 and AOM 400 (71.2% versus 70.9%, respectively). The most frequently reported TEAEs were increased weight (22.7% for Ari 2MRTU 960 versus 20.9% for AOM 400) and injection site pain (18.2% for Ari 2MRTU 960 versus 9.0% for AOM 400), none of which were assessed as serious or severe by the investigators. All injection site pain events in the Ari 2MRTU 960 group were assessed as mild or moderate in severity; most (15.9%) coincided with the first injection and resolved within 5 days. Extrapyramidal symptom scores remained unchanged in both treatment groups.
Conclusions. Multiple-dose administration of Ari 2MRTU 960 was generally well tolerated in patients with schizophrenia or BP-I and did not show any new safety concerns.
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Effect of Lumateperone (ITI-007) on Quality of Life and Functional Disability in the Treatment of Bipolar Depression

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Abstract

Introduction. In patients with bipolar disorder, depression symptoms are associated with greater reduction in function and quality of life than hypomania/mania symptoms. Lumateperone (LUMA), is an FDA-approved antipsychotic to treat schizophrenia and depressive episodes associated with bipolar I or bipolar II disorder.

In a recent phase 3 clinical trial (Study 404, NCT03249376) in people with bipolar depression, LUMA 42 mg monotherapy significantly improved symptoms of depression compared with placebo (PBO). This analysis of Study 404 investigated the effects of LUMA on functional disability and quality of life as measured using the secondary outcome measure, the Quality of Life Enjoyment and Satisfaction Questionnaire-Short Form (Q-LES-Q-SF).

Methods. Patients (18–75 years) with bipolar I or bipolar II disorder experiencing a major depressive episode (Montgomery-Åsberg Depression Rating Scale [MADRS] Total score ≥20 and Clinical Global Impression Scale-Bipolar Version-Severity [CGI-BP-S] score ≥4) were randomized to LUMA 42 mg or PBO orally, once daily in the evening for 6 weeks. The primary endpoint was the change from baseline to Day 43 in MADRS Total score, analyzed using a mixed-effects model for repeated measures (MMRM) approach in the intent-to-treat population (ITT). This post hoc analysis evaluated the mean change from baseline to Day 43 in the Q-LES-Q-SF individual item scores using an analysis of covariance with last observation carried forward (ANCOVA-LOCF) in the ITT. Categorical shifts in individual items were also analyzed.
Results. The ITT comprised 376 patients (LUMA 42 mg, 188; PBO, 188). Patients in the LUMA 42 mg group had significantly greater improvement on MADRS Total score change from baseline to Day 43 compared with PBO (least squares mean difference vs PBO [LSMD], −4.585; 95% CI, −6.344 to −2.826; effect size vs PBO [ES], −0.56; $P<.0001$). LUMA 42 mg treatment significantly improved Q-LES-Q-SF Total score from baseline to Day 43 compared with PBO (LSMD, 2.9; 95% CI, 1.15 to 4.59; $P=.001$).

The Q-LES-Q-SF items with the lowest mean scores at baseline in both groups were mood, leisure time activities, and sexual drive, interest, and/or performance. By Day 43, LUMA 42 mg treatment significantly improved 8 of the 14 items in the Q-LES-Q-SF ($P<0.05$). Overall life satisfaction also significantly improved with LUMA treatment ($P=.0016$). The largest improvements with LUMA 42 mg compared with PBO (ES>0.3,) were seen for the ability to function in daily life, family relationships, household activities, leisure time activities, and mood (all LSMD=0.3; all $P<.01$).
Conclusion. In patients with bipolar depression, treatment with LUMA 42 mg compared with PBO significantly improved patient quality of life and functional impairment. These results support LUMA 42 mg as treatment of MDEs associated with bipolar I or bipolar II disorder in adults.
Funding. Intra-Cellular Therapies, Inc.

Rhabdomyolysis Caused by a Behavioral Manifestation of Acute Mania

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Abstract

Introduction. While seen in patients with bipolar disorder due to NMS, antipsychotic side effects, or substance use, rhabdomyolysis resulting from behaviors seen in mania has not been reported in

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recent literature. We present a case of a patient with rhabdomyolysis due to exertion during a manic episode.

Case. A 29-year-old male with a history of bipolar disorder type 1 was brought to the ED in June 2022 after he was found on the roof of a local theater sharing excerpts from a book he had written. Temperatures outside were 100–102 Fahrenheit. On presentation, the patient had rapid, pressured speech and demonstrated flight of ideas. He was religiously preoccupied. He had been previously admitted to Psychiatric Emergency Services in April 2022 for mania and was discharged with lithium and lamotrigine. He had been titrating these medications with his outpatient psychiatrist.

The patient's labs showed an elevated creatinine of 1.49, up from his baseline of 1.09. Further workup revealed an elevated CK of 3,538. Additional abnormalities included an AST of 70, calcium of 10.6, total bilirubin of 1.6, and WBC of 15.5. He was afebrile, oriented, and had no obvious signs of infection. The patient received 2 liters of Lactated Ringers (LR) and was admitted to Internal Medicine. Later, he was agitated overnight and received 10mg olanzapine and 2mg lorazepam. Lithium level following fluid resuscitation was 0.6.

On interview the next day, the patient described working on a creative religious piece that he wanted to share with others, leading to him climbing on the roof. He had been hyper-focused on this work, with 1–4 hours of sleep nightly. He also had been frequently doing gymnastics, walking long distances, and climbing other buildings. He endorsed diffuse muscle pain, but this was not reproducible on exam.

150mL/hr of LR was started, and PO fluid intake was encouraged. He agreed to resume his medications and was started on lithium 900mg and lamotrigine 50mg. His CK continued to downtrend. WBC count decreased and was 12.9 at discharge. Lamotrigine was titrated up to home dose of 100mg. His mania improved, and he was ultimately discharged home with outpatient follow-up.

Conclusion. Rhabdomyolysis results from the release of toxic cellular compounds from muscle fibers. Complications include acute renal failure, hyperkalemia, and compartment syndrome. Causes include substance use, medications, trauma, seizures, ischemia, overexertion, and dehydration. Recently reported cases of mania-associated rhabdomyolysis involve iatrogenic causes, such as neuromuscular malignant syndrome (NMS) and non-NMS antipsychotic side effects.Other causes include high-risk drug use during mania. Rhabdomyolysis due to behavioral manifestations of mania have been documented more rarely in older reports, similarly, addressing excessive exercise and dehydration. Therefore, our case represents a reminder of the medical sequalae resulting from actions undertaken during acute mania. This highlights the importance of implementing effective treatment to prevent such episodes.

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A 16-Week Open-Label Study of the Effects of Treatment With Pimavanserin on Activities of Daily Living in Subjects With Parkinson's Disease Psychosis

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Abstract

Introduction. Accurate assessment of disability associated with Parkinson's Disease Psychosis (PDP) is essential and has been poorly studied. Patients often have poor insight on impact of PDP on daily function. This phase 4 study is the first to evaluate the impact of pimavanserin on activities of daily living (ADL) in PDP patients.

Methods. Eligible PDP patients entered a 16-week single-arm, open-label study of oral pimavanserin (34 mg) taken once daily. Primary endpoint (modified Functional Status Questionnaire [mFSQ]) and secondary endpoints (MDS-UPDRS I & II; Schwab and England ADL; CGI-S, CGI-I, and PGI-I) were measured as change from baseline to Week 16 using mixed-effects model for repeated measures (MMRM) and least-squares means (LSM).

Results. 29 patients were treated with pimavanserin, of which 24 (82.8%) completed the study. Treated patients demonstrated significant improvements in LSM (SE) mFSQ score change from baseline to Week 12 (11.5 [2.44]) and Week 16 (14.0 [2.50]; both $p<0.0001$). Significant improvements ($p<0.05$) were also observed for all secondary outcomes at Week 16 (MDS-UPDRS Part I: -6.3 [0.97]; MDS-UPDRS Part II: -2.6 [0.98]; CGI-S: -1.5 [0.25]; CGI-I: 1.9 [0.17]; PGI-I: 2.0 [0.22], except for Schwab and England ADL. No new safety signals were observed.

Conclusion. Functional outcomes and psychosis measures improved in PDP patients treated with pimavanserin, with safety findings consistent with previous studies. Our findings highlight the positive effect of pimavanserin in improving ADLs in patients with PDP.

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