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Cryptococcal Meningitis Leading to Fatal Outcomes in Immunocompetent Patients: A Case Study and Review of Literature

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ABSTRACT: Introduction: Cryptococcal Meningitis is a fungal infectious disease of worldwide distribution, primarily associated with underlying immunosuppression conditions such as HIV infection, glucocorticoid treatment, status post organ transplantation and oncological treatments. Prevalence is particularly high in third-world countries where it constitutes one of the primary causes of central nervous system infections and may carry fatal outcomes. We present two cases of Cryptococcal Meningitis that portray the vast spectrum of clinical presentations associated with Cryptococcal Meningitis as well as relevant diagnostic and therapeutic implications.

METHODS: Case study - These adult otherwise healthy patients presented at a public urban university hospital in southern Colombia. Both had an unusual clinical course and suffered fatal outcomes despite being seemingly immunocompetent at baseline. A diagnosis of hepatic cirrhosis could have been considered a cause of immunosuppression in one of the patients and the diagnostic work-up for the other patient revealed no evidence of immunological deficiency.

DISCUSSION: Cryptococcal Meningitis affecting immunocompetent individuals has been increasingly reported in recent years. Furthermore, outcomes in this population are particularly worse than those generally affected by the disease. A review of the literature related to the possible immunological mechanisms' underlying the presented clinical course is included. We emphasize the importance of considering Cryptococcus spp. as a possible etiologic agent among differential diagnoses upon encountering suggestive meningeal conditions in immunocompetent patients.

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Lumateperone (ITI-007) for the Treatment of Schizophrenia: Overview of Placebo-Controlled Clinical Trials and an Open-label Safety Switching Study

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ABSTRACT: Background: Lumateperone is a first-in-class agent in development for schizophrenia that acts synergistically through serotonergic, dopaminergic and glutamatergic systems. Lumateperone is a potent 5-HT2A antagonist, a mesolimbic/mesocortical dopamine phosphoprotein modulator (DPPM) with presynaptic partial agonist and post-synaptic antagonist activity at D2, a glutamate GluN2B receptor phosphoprotein modulator with D1-dependent enhancement of both NMDA and AMPA currents via the mTOR protein pathway and an inhibitor of serotonin reuptake.

METHODS: Lumateperone was evaluated in 3 controlled clinical trials to evaluate efficacy in patients with acute schizophrenia. The primary endpoint was change from baseline on the PANSS total score compared to placebo. In Study '005, 335 patients were randomized to receive ITI-007 60 mg or 120 mg , risperidone 4 mg (active control) or placebo QAM for 4 weeks. In Study '301, 450 patients were randomized to receive ITI-007 60 mg or 40 mg , or placebo QAM for 4 weeks. In Study '302, 696 patients were randomized to receive ITI-007 60 mg or 20 mg , risperidone 4 mg (active control) or placebo QAM for 6 weeks. Also, an open-label safety switching study was conducted in which 302 patients with stable schizophrenia were switched from standard-of-care (SOC) antipsychotics and treated for 6 weeks with lumateperone QPM and then switched back to SOC.

RESULTS: In Studies '005 and '301, lumateperone (60 mg ITI-007) met the primary endpoint with statistically significant superior efficacy over placebo at Day 28. In Study '302, neither dose of lumateperone separated from placebo on the primary endpoint; a high placebo response was observed in this study. Across all 3 efficacy