Cardiometabolic Safety of Lumateperone (ITI−007): Post Hoc Analyses of Short-Term Randomized Trials and an Open-Label Long-Term Study in Schizophrenia

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Abstract

Study Objective. Current treatments for schizophrenia are often associated with increased rates of metabolic syndrome (MetSy). MetSy is defined as meeting 3 of the following 5 criteria: waist circumference >40in (men) or >35in (women), triglycerides =150mg/dL, high density lipoprotein cholesterol (HDL) <40mg/dL (men) or <50mg/dL (women), systolic blood pressure (BP) =130mmHg or diastolic BP =85mmHg, fasting glucose =100mg/dL. Patients with MetSy have an elevated risk of developing type II diabetes and increased mortality due to cardiovascular disease. 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. This distinct pharmacological profile has been associated with favorable tolerability and a low risk of adverse metabolic effects in clinical trials. This post hoc analysis of 2 randomized, double-blind, placebo-controlled studies of patients with an acute exacerbation of schizophrenia compared rates of MetSy with lumateperone and risperidone. Data from an open-label long-term trial of lumateperone were also evaluated.

Method. The incidence and shift in MetSy were analyzed in data pooled from 2 short-term (4 or 6 week) placebo- and active-controlled (risperidone 4mg) studies of lumateperone 42mg (Studies 005 and 302). The pooled lumateperone data were compared with data for risperidone. Data from an open-label 1-year trial (Study 303) evaluated MetSy in patients with stable schizophrenia switched from prior antipsychotic (PA) treatment to lumateperone 42mg.

Results. In the acute studies (n=256 lumateperone 42mg, n=255 risperidone 4mg), rates of MetSy were similar between groups at baseline (16% lumateperone, 19% risperidone). At the end of treatment (EOT), MetSy was less common with lumateperone than with risperidone (13% vs 25%). More lumateperone patients (46%) compared with risperidone (25%) patients improved from having MetSy at baseline to no longer meeting MetSy criteria at EOT. Conversely, more patients on risperidone than on lumateperone developed MetSy during treatment (13% vs 5%). Differences in MetSy conversion rates were driven by changes in triglycerides and glucose. In the long-term study (n=602 lumateperone 42mg), 33% of patients had MetSy at PA baseline. Thirty-six percent of patients (36%) with MetSy at PA baseline improved to no longer meeting criteria at EOT. Fewer than half that percentage shifted from not meeting MetSy criteria to having MetSy (15%).

Conclusions. In this post hoc analysis, lumateperone 42mg patients had reduced rates of MetSy compared with risperidone patients. In the long-term study, patients with MetSy on PA switched to lumateperone 42mg had a reduction in the risk of MetSy. These results suggest that lumateperone 42mg is a promising new treatment for schizophrenia with a favorable metabolic profile.

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Knowledge of The Recognition and Management of Tardive Dyskinesia Markedly Improved Among Psychiatrists: Assessing the Impact of Online Medical Education

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Abstract

Introduction. Tardive dyskinesia (TD) is a persistent and potentially disabling movement disorder associated with prolonged exposure to antipsychotic medications that jeopardizes adherence to treatment and reduces quality of life. The recognition and management of TD can be challenging in many instances. An online activity was developed to assess the ability of continuing medical education (CME) to improve awareness of the recognition and management of TD among psychiatrists.

Methods. The online CME activity consisted of a 30-minute video discussion between three expert faculty. Educational effect was assessed by comparing a matched sample of psychiatrists' responses to four identical questions pre- and post-activity. A chi-square test identified significant differences between pre- and post-assessment responses. Cramer's V was used to calculate the effect size of the online education ($\geq$ 0.16 is considerable). Data were collected between June 26 and August 6, 2019.

Results. Activity participation resulted in a considerable educational effect among psychiatrists (n=739; V=0.25, P<0.001). The following areas showed significant (P <0.05) pre- vs post-