Cognitive Functioning and Acute Sedative Effects of Risperidone and Quetiapine in Patients With Stable Bipolar I Disorder: A Randomized, Double-Blind, Crossover Study

Philip D. Harvey, Ph.D.; Howard Hassman, D.O.; Lian Mao, M.S.; Georges M. Gharabawi, M.D.; Ramy A. Mahmoud, M.D., M.P.H.; and Luella M. Engelhart, M.A.

Objective: Antipsychotic medications differ in their sedative potential, which can affect cognitive performance. The primary objective of this double-blind study was to compare the effects of treatment initiation with risperidone and quetiapine on cognitive function in subjects with stable bipolar disorder.

Method: Subjects had a DSM-IV diagnosis of bipolar I disorder in partial or full remission and a Young Mania Rating Scale score ≤ 8 at screening. Subjects were randomly assigned to 1 of 2 treatment sequences: risperidone-quetiapine or quetiapine-risperidone. Subjects in the risperidone-quetiapine sequence received 2 mg of risperidone with dinner and placebo with breakfast during period 1 and 100 mg of quetiapine with dinner and 100 mg with breakfast during period 2. Subjects in the quetiapine-risperidone sequence received the same treatments in reverse order. The 2 treatment periods were separated by a 6- to 14-day washout period. Cognitive function, including attention, working memory, declarative memory, processing speed, and executive functions, was measured before and after dosing. The Visual Analog Scale for Fatigue was also completed. The primary endpoint was a neurocognitive composite score (NCS). The study was conducted from November 2004 through August 2005.

Results: Thirty subjects were randomly assigned; 28 took all doses of study medication and completed a baseline and at least 1 postbaseline assessment in each treatment. On the NCS, significantly better overall cognitive function was seen after risperidone than after quetiapine at each time point after dosing. Subjects performed significantly better after risperidone than after quetiapine on 9 of the 18 individual cognitive outcome measures and significantly better after quetiapine than after risperidone on 1 measure. Sleeping or the need for sleep during the test days was reported in significantly more patients after receiving quetiapine than risperidone.

Conclusions: The results indicate that initiation of quetiapine treatment was associated with more immediate adverse cognitive effects and increased somnolence than risperidone treatment.

Clinical Trials Registration:
ClinicalTrials.gov identifier NCT00097032.

Received June 30, 2006; accepted Jan. 2, 2007. From the Department of Psychiatry, Mt. Sinai School of Medicine, New York, N.Y. (Dr. Harvey); the CNS Research Institute, Clementon, N.J. (Dr. Hassman); Ortho-McNeil Janssen Scientific Affairs, L.L.C., Titusville, N.J. (Mr. Mao and Ms. Engelhart); and Medical Affairs, Janssen Pharmaceuticals, Inc., Titusville, N.J. (Drs. Gharabawi and Mahmoud). Dr. Gharabawi is now employed by Hoffman-La Roche, Inc., Nutley, N.J., and Ms. Engelhart is now employed by Cordis Corporation, Warren, N.J.

The study was funded by Ortho-McNeil Janssen Scientific Affairs, L.L.C.

Dr. Harvey serves as a consultant for Janssen, Eli Lilly, AstaZeneica, Pfizer, and Bristol-Myers Squibb; has received research grants from Bristol-Myers Squibb, Pfizer, and Ortho-McNeil Janssen Scientific Affairs; and is a member of the speakers/advisory boards for Eli Lilly and Pfizer. Mr. Mao is an employee of Ortho-McNeil Janssen Scientific Affairs. Dr. Gharabawi and Dr. Mahmoud are employees of Janssen and stock shareholders of Johnson & Johnson. Ms. Engelhart is an employee of Ortho-McNeil Janssen Scientific Affairs and a stock shareholder of Johnson & Johnson. Dr. Hassman was the principal investigator for the study and reports no additional financial or other relationships relevant to the subject of this article.

Corresponding author and reprints: Luella Engelhart, Health Economics and Outcomes Research, Cordis Corporation, 7 Powder Horn Dr, Warren, NJ 07059 (e-mail: lengelh2@cordis.com).

Medication-induced sedation is associated with drowsiness, reduced wakefulness, slowed brain activity, and impaired cognitive performance1 and thus can be problematic for many persons who are employed, operate a motor vehicle, or have other responsibilities. Somnolence has been reported as a prominent adverse event in bipolar patients receiving risperidone or quetiapine, both as monotherapy and as an adjunct to mood stabilizers, for the treatment of bipolar mania.2–9 Somnolence in these studies was recorded only from the patients’ self-reports and its incidence tended to vary from study to study. Moreover, the severity of somnolence was not