# Late Breaking Clinical Trials

## Quetiapine as Potential First-Line Treatment in Acute Bipolar II Depression

Patients with bipolar II disorder can be particularly difficult to treat, as they are sensitive to the side effects of treatment and more susceptible to treatment-emergent rapid cycling and shifts in affect. Currently there is not enough evidence to select one agent over another in terms of first-line therapy. Michael Thase, MD, University of Pennsylvania, presented results of quetiapine monotherapy in the treatment of acute depression in patients with bipolar II disorder. "Bipolar II disorder is dominated by the depressive phase of the illness, and in fact people with bipolar II spend half of their adult lives with depressive symptoms," said Dr. Thase. Quetiapine is indicated for the treatment of schizophrenia, depressive episodes in bipolar disorder, and as an adjunctive medication in manic episodes of bipolar I disorder. Two randomized, placebo-controlled, pivotal trials (BOLDER I and BOLDER II) were conducted to assess the efficacy and tolerability of quetiapine in bipolar I and bipolar II depression (Calabrese JR et al. *Am J Psychiatry* 2005;162(7):1351-60; Thase ME et al. *J Clin Psychopharmacol* 2006;26(6):600-9). These two studies enrolled 1,045 patients, of which 351 had bipolar II disorder. These data presented an opportunity to further analyze the subset of subjects with bipolar II depression. The studies lasted 8 weeks and patients received either quetiapine 300 or 600 mg/day or placebo. The primary outcome measure was the change from baseline to final in the Montgomery Asberg Depression Scale (MADRS) score.

A total of 118 patients received quetiapine 300 mg/day, 116 received quetiapine 600 mg/day and 117 received placebo; 61% completed. The 3 treatment groups were similar demographically. Both doses of quetiapine were significantly effective in reducing MADRS scores over time in the patients with bipolar II depression. The quetiapine groups demonstrated statistically significant differences compared to placebo as early as one week after initiation of treatment, and this differentiation was maintained throughout the 8-week study. Additionally, quetiapine-treated patients had significant improvements compared to placebo at the final evaluation in HAM-D, HAM-A, and CGI-S scores (all $p<0.01$). Adverse events experienced by >10% in any treatment group included dry mouth, sedation, somnolence, dizziness, fatigue, constipation, and headache. Treatment-emergent rates of mania were low and comparable between treatments, with 1.7% in the quetiapine 300 mg/day group, 2.6% with quetiapine 600 mg/day, and 2.6% in those taking placebo. "The data suggest that quetiapine should be a first-line therapy" for bipolar II depression, said Dr. Thase, although he admitted that gathering long-term data is warranted. The data from this presentation is in press (Suppes et al. *World J Biol Psych*).

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