

Predictors of Early Relapse in Manic and Mxed-manic Patients with Olanzapine or Placebo

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Background: Early relapse within the first few months of stabilization of an acute episode in bipolar disorder might be preventable with better vigilance and quicker intervention. Since symptoms often emerge or worsen prior to relapse, we sought specific ones that may have predictive ability for mania relapse from a blinded, bipolar I disorder relapse prevention study of olanzapine versus placebo.

Methods: Post-hoc analysis was conducted on Young Mania Rating Scale (YMRS) item scores prospectively collected weekly and biweekly in 323 euthymic (YMRS \leq 12 and Hamilton Depression Score \leq 8) patients initially stabilized on olanzapine and randomized to olanzapine (n=213, 5-20 mg/day) or placebo (n=110). To minimize possible withdrawal effects in placebo-treated patients, only data for relapses that occurred 2-8 weeks after randomization were analyzed. Repeated measures logistic regression analysis of detectable changes (increase in an item score of 1 or more) in YMRS ratings during the 1-2 week visit interval prior to relapse (YMRS total score \geq 15 or hospitalization) was used to estimate odds of relapse by the next visit.

Results: Within the 2- to 8-week period post randomization, 44 patients relapsed (olanzapine, n=18; placebo, n=26). Increases in YMRS item scores preceding manic relapse were (olanzapine, placebo, respectively): decreased sleep need (33.3%, 42.3%), increased motor activity/energy (33.3%, 26.9%), and increased speech (amount/rate) (27.8%, 15.4%). YMRS items with the largest odds ratios for relapse prediction were: disheveled appearance (7.1, $p < .001$), decreased sleep (5.8, $p < .001$), increased motor activity/energy (5.6, $p < .001$), and disruptive aggressive behavior (5.5, $p = .004$) in olanzapine-treated patients, and disruptive aggressive behavior (3.9, $p = .013$), decreased sleep (3.2, $p = .007$), and increased motor activity/energy (3.0, $p = .023$) in placebo-treated patients. Overall, 77.8% olanzapine-treated and 76.9% placebo-treated patients had pre-relapse increases in at least one YMRS item with significant odds ratios of 5.3 ($p = .004$) and 3.9 ($p = .005$) respectively.

Conclusions: Decreased need for sleep, increased aggressive behavior, and increased psychomotor activity frequently preceded and significantly predicted relapse within two weeks in patients treated with either olanzapine or placebo.