Article: 2288
Topic: 40 - Bipolar Disorders

A 12-WEEK, RANDOMIZED, PLACEBO-CONTROLLED STUDY EVALUATING THE EFFICACY AND SAFETY OF ARIPIPRAZOLE IN COMBINATION WITH LITHIUM/VALPROATE IN PARTIALLY-RESPONSIVE BIPOLAR MANIA

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Objective: Evaluate the efficacy of aripiprazole combination with lithium/valproate vs. placebo combination in bipolar mania using a titration regimen with a low starting dose (5mg/day).
Methods: Eligible adult patients with bipolar mania receiving lithium/valproate and a Young Mania Rating Scale (YMRS) Total score ≥16 who might benefit from combination treatment with aripiprazole, were randomized to aripiprazole (n=181) or placebo (n=189) with lithium/valproate. Primary endpoint was mean change from baseline to Week 12 in YMRS. Secondary endpoints were Clinical Global Impressions-Bipolar Version (CGI-BP) severity of illness score, response rate (≥50% improvement in YMRS Total score), and remission rate (YMRS ≤12). Safety and tolerability were also assessed. Enrolment yielded a 77% power to detect a 2.6-point change in YMRS Total score at endpoint.
Results: At endpoint, the mean change in YMRS Total Score (last-observation-carried-forward [LOCF]) for aripiprazole vs. placebo was not significant (treatment difference [-2.04] in favour of aripiprazole (95% CI: -4.14, 0.07; p=0.058). Mean change from baseline to endpoint in CGI-BP showed a treatment difference (-0.30) in favour of aripiprazole vs. placebo (95% CI: -0.59, -0.01; p=0.044). Response rates were 68.8% vs. 61.3% (p=0.128) and remission rates were 69.9% vs. 64.0% (p=0.211) for aripiprazole and placebo, respectively. No unexpected adverse events (AEs) occurred. Treatment-emergent AEs (≥5% and twice the rate of placebo) were akathisia, depression, and nausea.
Conclusions: The target sample size of 388 patients was not achieved in this study and the primary outcome did not reach statistical significance. Now new or unexpected AEs occurred.

https://doi.org/10.1016/S0924-9338(13)77147-5 Published online by Cambridge University Press