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ABSTRACT: Study Objectives: To report functional recovery, symptomatic remission, and sustained symptomatic remission rates after treatment with aripiprazole once-monthly 400 mg (AOM 400) administered every 4 weeks for up to 52 weeks as maintenance treatment in a mixed cohort of AOM 400 naïve (de novo) and experienced adults (rollover) with bipolar I disorder (BP-I).

METHOD: This open-label study (NCT01710709) enrolled de novo patients with a diagnosis of BP-I and ≥1 previous manic or mixed episode and rollover patients who completed a randomized, double-blind, placebo-controlled study assessing the efficacy and safety of AOM 400 (NCT01567527). Efficacy was assessed by mean changes from baseline in Young-Mania Rating Scale (YMRS), Montgomery-Asberg Depressive Rating Scale (MADRS), and Clinical Global Impression- Bipolar Version-Severity of Illness (CGI-BP-S) scores. Sustained functional recovery was defined as a total score of ≤11 on the Functioning Assessment Short Test (FAST) for ≥8 consecutive weeks. Remission was defined as YMRS and MADRS total scores ≤12, and sustained remission was defined as meeting criteria for remission for 8 consecutive weeks. The study included a screening phase (6 weeks) for de novo patients, an oral aripiprazole conversion phase (4–6 weeks), an oral stabilization phase (4–12 weeks), and an AOM 400 maintenance phase (up to 52 weeks). Rollover patients entered directly into the AOM 400 maintenance phase.

RESULTS: A total of 464 subjects entered the maintenance phase and 63% (291/464) completed the trial. Of patients entering the maintenance phase, 379 (82%) were de novo and 85 (18%) were rollover. The most frequent reasons for discontinuation were withdrawal of consent (11%) and adverse events (AEs) (10%). Weight increase (1.5%, 7/464) and BP-I (0.9%, 4/464) were the most common reasons for discontinuation due to AEs. Improvements in mean YMRS, MADRS, CGI-BP-S, and FAST scores achieved in previous phases were maintained over 52 weeks. Treatment-emergent AEs experienced by >10% of the patients were akathisia (14.7%), weight increased (13.4%), nasopharyngitis (12.1%), and insomnia (11.0%). A high proportion of de novo patients met the criteria for symptomatic remission (87.2%, 328/376) and sustained remission (77%, 292/379) by last visit. Rollover patients' remission rate remained stable (98.8%, 84/85) by last visit. Of the rollover patients, 35/85 (43%) and 35/116 (36%) of de novo subjects met the criteria for sustained functional recovery after study completion.

CONCLUSIONS: Patients treated with AOM 400 maintained symptomatic and functional stability for up to 52 weeks. Importantly, more than one-third of patients achieved sustained functional recovery using a strict criterion. Overall, AOM 400 was safe and well tolerated in patients with BP-I. Results support AOM 400 as a viable once-monthlyoption for maintenance treatment of BP-I.

These data were previously presented at the 31st ECNP Congress, 2018, Barcelona, Spain.
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Combinatorial Pharmacogenomics to Guide Treatment Selection for Major Depressive Disorder: A Large, Blinded, Randomized Controlled Trial

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ABSTRACT: Background: Major depressive disorder (MDD) is a leading cause of disease burden worldwide, with lifetime prevalence in the United States of 17%. Here we present the results of the first prospective, large-scale, patient- and rater-blind, randomized controlled trial evaluating the clinical importance of achieving congruence between combinatorial pharmacogenomic (PGx) testing and medication selection for MDD.

METHODS: 1,167 outpatients diagnosed with MDD and an inadequate response to ≥1 psychotropic medications were enrolled and randomized 1:1 to a Treatment as Usual (TAU) arm or PGx-guided care arm. Combinatorial PGx testing categorized medications in three groups based on the level of gene-drug interactions: use as directed, use with caution, or use with increased caution and more frequent monitoring. Patient assessments were performed at weeks 0 (baseline), 4, 8, 12 and 24. Patients, site raters, and central raters were blinded in both arms until after week 8. In the guided-care arm, physicians had access to the combinatorial PGx test result to guide medication selection. Primary outcomes utilized the Hamilton Depression Rating Scale (HAM-D17) and included symptom improvement (percent change in HAM-D17 from baseline), response (50% decrease in HAM-D17 from baseline), and remission (HAM-D17 <7) at the fully blinded week 8 time point. The durability of patient outcomes was assessed at week 24. Medications were considered congruent with PGx test results if they were in the 'use as directed' or 'use with caution' report categories while medications in the 'use with increased caution and more frequent monitoring' were considered incongruent. Patients who started on incongruent medications were analyzed separately according to whether they changed to congruent medications by week 8.

RESULTS: At week 8, symptom improvement for individuals in the guided-care arm was not significantly different than TAU (27.2% versus 24.4%, $p = 0.11$). However, individuals in the guided-care arm were more likely than those in TAU to achieve remission (15% versus 10%; $p < 0.01$) and response (26% versus 20%; $p = 0.01$). Remission rates, response rates, and symptom reductions continued to improve in the guided-treatment arm until the 24 week time point. Congruent prescribing increased to 91% in the guided-care arm by week 8. Among patients who were taking one or more incongruent medication at baseline, those who changed to congruent medications by week 8 demonstrated significantly greater symptom improvement ($p < 0.01$), response ($p = 0.04$), and remission rates ($p < 0.01$) compared to those who persisted on incongruent medications.

CONCLUSIONS: Combinatorial PGx testing improves short- and long-term response and remission rates for MDD compared to standard of care. In addition, prescribing congruency with PGx-guided medication recommendations is important for achieving symptom improvement, response, and remission for MDD patients.
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Adjunctive Buprenorphine/Samidorphan Combination in Patients with Major Depressive Disorder: Phase 3 Long-term Extension Study Results

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ABSTRACT: Introduction: Buprenorphine/samidorphan (BUP/SAM), a combination of BUP (a μ-opioid receptor

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