# Long-Term Efficacy of Combination Therapy of Transcranial Magnetic Stimulation with Ketamine for Patients with Treatment-Resistant Depression

Steve Best, MD[1], Dan G. Pavel, MD[2] and Natalie Haustrup, PhD[3]

[1]The Neuroscience Center, Director, Deerfield, IL, USA, [2]PathFinder Brain SPECT Imaging, Director, Deerfield, IL, USA, and [3]Haustrup Scientific Consulting, Cork, Ireland

**Presenting Author:** Steve Best, Dan Pavel, Natalie Haustrup

## Abstract

**Background.** Repetitive transcranial magnetic stimulation (rTMS) is a safe, effective and non-invasive treatment for many psychiatric illnesses, including treatment-resistant depression (TRD). Ketamine, an NMDA receptor antagonist, is also an effective antidepressant. This retrospective review examined the clinical benefits of combining these two established treatments for patients suffering from TRD in a novel approach coined combination TMS with ketamine (CTK).

**Methods.** A group of 28 adult patients with a primary diagnosis of unipolar (n=18) or bipolar (n=10) depression received three CTK treatments a week at a private neuropsychiatric practice. Patients were given a concurrent treatment of rTMS (1Hz; 40 minutes; 130% of motor threshold) with bio-marker-determined IV ketamine infusions (0.2–4.7 mg/kg; 30 minutes). The TMS coil was positioned on the mid-prefrontal area. Frequency of treatment was dependent on patient responsiveness (10–30 sessions), which was measured as symptom reduction on the Clinical Global Impression (CGI) scale. CGI data was evaluated pre-treatment, post-treatment and at two-year follow-up.

**Results.** Mean reduction in CGI severity for the patient group following CTK was $4.46 \pm 0.54$ at a 99% confidence interval and was deemed statistically significant using a paired t-test ($a=0.01$, $t=22.81$, $p < 0.0001$). This significant reduction in CGI severity was sustained for at least 2 years following treatment completion.

**Conclusions.** Despite years of unsuccessful treatments, all 28 patients in this trial obtained substantial and enduring reductions in their depressive symptoms following CTK therapy. Further research into method optimization and randomized controlled trials are warranted.

# Aripiprazole Lauroxil 2-Month Formulation With 1-Day Initiation for Acute Schizophrenia: ALPINE Exploratory Efficacy and Patient-Reported Outcomes

Henry Nasrallah, MD[1], David Walling, MD[2], Peter J. Weiden, MD[3], Yangchun Du, PhD[3], Baiyun Yao, PhD[3], Sergey Yagoda, PhD[3] and Amy Claxton, PhD[3]

[1]University of Cincinnati College of Medicine, Cincinnati, OH, USA, [2]CNS Network, LLC, Garden Grove, CA, USA, and [3]Alkermes, Inc., Waltham, MA, USA

**Presenting Author:** Amy Claxton

## Abstract

**Objective.** The randomized, controlled, phase 3b ALPINE study evaluated efficacy and safety of a 2-month formulation of aripiprazole lauroxil (AL) initiated with a 1-day regimen during hospitalization for an acute exacerbation of schizophrenia; paliperidone palmitate (PP) was included as an active control. The primary efficacy outcome, within-group change from baseline in PANSS total score at 4 weeks, was previously reported. Here we report additional exploratory PANSS subscale endpoints and patient-reported outcomes (PROs).

**Methods.** Adults aged 18–65 years were enrolled as inpatients and randomized to AL 1064 mg q8wk or PP 156 mg q4wk and discharged after 2 weeks of study treatment if clinically stable. Patients were followed as outpatients through week 25. Exploratory efficacy endpoints were PANSS subscale (Positive, Negative, and General) and Clinical Global Impression-Severity (CGI-S) scores. The Burden Assessment Scale was administered to patients' nonprofessional caregivers (family member or friend). Exploratory PROs (Quality of Life Enjoyment and Satisfaction Questionnaire Short Form [Q-LES-Q-SF] and Medication Satisfaction Questionnaire) were assessed during the outpatient period. Within-group changes in PANSS subscales and CGI-S scores from baseline through week 25 were analyzed for AL and PP using mixed models with repeated measures. PROs were summarized based on observed data.

**Results.** In total, 200 patients were randomized (AL, n=99; PP, n=101); 99 (AL, n=56; PP, n=43) completed the 25-week study. PANSS Positive, Negative, and General subscale scores improved with AL treatment as measured by change from baseline to week

https://doi.org/10.1017/S1092852920002795 Published online by Cambridge University Press

25 (least squares [LS] mean [95% CI]: Positive, −7.0 [−8.1, −6.0]; Negative, −3.7 [−4.7, −2.8]; General, −11.1 [−12.7, −9.5]), as did CGI-S scores (LS mean [95% CI] change at week 25: –1.2 [–1.4 –1.0]). Caregiver burden decreased over the treatment period, with the largest decline noted at week 9 for AL patients' caregivers (mean change from baseline at week 9: −8.4; week 25: −8.9). Over weeks 5, 9, and 17, 70.8%−74.7% of AL-treated patients were somewhat or very satisfied with treatment. Mean Q-LES-Q-SF total scores were stable. With PP, PANSS subscale and CGI-S scores improved from baseline to study end (LS mean [95% CI] changes at week 25: Positive, −7.1 [−8.2, −5.9]; Negative, −3.5 [−4.6, −2.5]; General, −10.4 [−12.1, −8.6]; CGI-S, −1.2 [−1.5, −1.0]). Mean caregiver burden decreased (week 9: −8.8; week 25: −9.2). Most PP patients were satisfied or very satisfied with treatment (64.7%−69.3% at weeks 5, 9, and 17), and mean Q-LES-Q-SF total scores were stable.

**Conclusion.** In ALPINE, patients who initiated AL or PP in the hospital and continued treatment during outpatient care experienced improvement in schizophrenia symptoms and reported satisfaction with medication, decreased caregiver burden, and stable quality of life.

**Funding.** Alkermes, Inc.

# Treating Comorbid Childhood Bipolar Disorder and ADHD

Darlyne G. Nemeth, PhD, MP, MPAP, Kayla M. Chustz, BS and Cody M. Capps, BS

Neuropsychology Center of Louisiana, Baton Rouge, LA, USA

**Presenting Author:** Cody Capps

## Abstract

**Objectives.** Pediatric mania is difficult to distinguish from childhood hyperactivity. Both share 3 common symptoms: distractibility, motoric hyperactivity, and talkativeness. Oftentimes, children are referred from their pediatrician due to a lack of appropriate response to stimulant medication. Pediatricians have learned that merely raising the dose or changing the stimulant does not work. A thorough neuropsychological evaluation often reveals bipolar mania. They may have comorbid bipolar disorder and ADHD. This poster paper will examine measures that can assist in this important differential diagnosis as well as offer treatment options, including medication management.

**Methods.** This case study includes three pediatric patients diagnosed with childhood bipolar disorder and ADHD. A comprehensive psychoeducational assessment was conducted for each of the patients, which resulted in this comorbid diagnosis.

**Results.** One of the most helpful measures was the TOVA (i.e., Test of Variables of Attention). When a child's attention and impulsivity scores are normal, and response time and variability scores are abnormal, both on and off medication, that is an indication of a mood disorder, These children also performed poorly on measures of processing speed, and verbal learning and interference tasks. Measures of affect and personality were important diagnostically. A combination of amantadine and either clonidine HCL ER or propranolol, as prescribed by a medical psychologist, were found to be effective in controlling the symptoms of this comorbid diagnosis.

**Conclusions.** An evaluation of children's intellectual, attentional, behavioral, mood, and personality functioning is crucial for a differential diagnosis. In cases of comorbidity, ADHD and childhood bipolar disorder, the sooner the child is on appropriate medications, the better. When just the surface diagnosis of ADHD is medicated, the outcome is often problematic. There may be a poor response to treatment and a higher rate of suicide.

# Hospitalization Risk Among Adults with Bipolar I Disorder Treated with Oral Atypical Antipsychotics: A Long-Term Data Analysis of Medicaid Claims Data

Xiaoli Niu, PhD[1], Phani Veeranki, MD, DrPH[2], Syvart Dennen, MS[2], Yanmei Liu, MS[2], Jason Shafrin, PhD[2], Carole Dembek, MS[1], Kimberly Laubmeier, PhD[1] and G. Rhys Williams, DSc[1]

[1]Sunovion Pharmaceuticals Inc., Marlborough, MA, USA, and [2]PRECISIONheor, Los Angeles, CA, USA

**Presenting Author:** Kimberly Laubmeier

## Abstract

**Objective.** To compare the risk of hospitalization for adult Medicaid beneficiaries with bipolar I disorder (BPD-I) when treated with lurasidone compared to other atypical antipsychotics (AAPs) as monotherapy.

**Methods.** Using IBM MarketScan Multi-State Medicaid Claims database, a retrospective cohort study was conducted on adult BPD-I patients who initiated an AAP (index date) between January 1, 2014 and June 30, 2019. Patients were required to be continuously enrolled during the 12-month pre- and 24-month post-index date. Marginal structural models were performed to estimate the risk of hospitalization (all-cause, BPD-I-related, and psychiatric-related) associated with each AAP and the average length of stay.

**Results.** The analysis included 8262 adult BPD-I patients, of whom AAP use was divided between lurasidone (14%), aripiprazole (17%), olanzapine (8%), quetiapine (29%), risperidone (10%), no/minimal (1%) or other (21%) during each month of post-index period. The adjusted odds ratios (aORs) for all-cause hospitalization were significantly higher for olanzapine (aOR=1.60, 95% CI=1.09–2.10) and quetiapine (aOR=1.54, 95% CI=1.18–1.89), compared to lurasidone. The aORs for BPD-I-related hospitalization were significantly higher for quetiapine (aOR=1.57, 95% CI=1.10–2.04) and risperidone (aOR=1.80, 95% CI=1.04–2.56) compared to lurasidone. The average length of hospital stay was more than twice as high for quetiapine compared to lurasidone (aRR=2.12, 95% CI=1.32–2.92). The risk of psychiatric-related hospitalization was numerically lower for lurasidone compared to all other AAPs.

**Conclusion.** Over a 24-month follow-up period, lurasidone-treated adult BPD-1 patients had significantly lower risk of all-

https://doi.org/10.1017/S1092852920002795 Published online by Cambridge University Press