Abstract

Background. Schizophrenia affects individuals, families, and systems, with treatment primarily being antipsychotic medications. Long-acting injectable (LAI) antipsychotics are increasingly being used. This study sought to identify predictors of antipsychotic choice, in terms of formulation (LAI vs oral) and class (FGA vs SGA), and clinical outcomes.
Methods. 123 patients who received LAI antipsychotics were diagnosis-matched to patients who received oral antipsychotics. Sociodemographic and clinical factors were extracted from the medical record, including indicators of illness severity. Groups were compared with Chi-Square and t-tests, and logistic regression models were used to identify independent predictors of antipsychotic choice.
Results. Patients that received LAIs had longer admissions, more complex discharges, and greater illness severity; however, there were no differences in readmission rates. Independent predictors of LAIs included younger age, being single, and longer admission. Patients who received FGA LAIs were more likely to use substances and be undomiciled compared to SGA LAIs, with the only predictor being older age. Oral FGAs were more likely than oral SGAs to be prescribed to older and female patients, as well as those with co-occurring substance use, complex discharges, and longer admissions.
Conclusions. Illness severity and duration of illness appear to drive choice of LAI vs. oral antipsychotic medication and FGA vs. SGA. While LAIs were prescribed to patients with greater illness severity, readmission rates were equivalent to those receiving oral medication, supporting the use of LAI in patients with greater illness severity. Rationales for prescribing LAIs to younger patients and FGAs to older patients are discussed.
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Complete in vitro Dissolution of Valbenazine as Either Whole Capsules or Crushed Capsule Contents

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Abstract

Introduction. Tardive dyskinesia (TD) is a persistent and potentially disabling movement disorder associated with exposure to antipsychotics and other dopamine receptor blocking agents. Three valbenazine capsule strengths (40 mg, 60 mg, 80 mg) are approved for the once-daily treatment of TD. However, some patients with TD, especially in elderly populations, have trouble swallowing due to orolingual movements. This study was conducted to evaluate two different dissolution methods for valbenazine: whole intact capsules versus crushed capsule contents.
Methods. Samples were prepared using two commercial lots (Lot-A, Lot-B) for two doses (40 mg, 80 mg), with six replicate samples per lot and dose. The whole capsules were weighed, put into a sinker, and added to a dissolution bath containing 900 mL of 0.1N HCl at 37±0.5° Celsius. Testing on the crushed capsule contents commenced after opening the capsules, weighing and crushing the contents, and transferring the contents to the dissolution bath. Samples were collected (at 10, 15, 20, 30, 45, and 60 min) with a paddle speed of 50 rpm and analyzed using high performance liquid chromatography. Standards were prepared at nominal concentrations of 0.044 mg/mL (for 40 mg) and 0.089 mg/mL (for 80 mg).
Results. Capsules were opened easily by manual manipulation, and contents were crushed easily between spoons. Very rapid (>85% in 15 min) and complete drug release was observed in all samples, independent of capsule strength (40 mg, 80 mg) or preparation (whole intact capsule or crushed capsule contents). For 40-mg capsules, average percent release at first and last collection timepoints were as follows (whole vs crushed): 10 min (98.4% vs 98.6% [A], 93.7% vs 97.6% [B]); 60 min (102.3% vs 100.5% [A], 100.9% vs 100.6% [B]). Results for 80-mg capsules were as follows: 10 min (98.2% vs 99.6% [A], 99.4% vs 97.9% [B]); 60 min (102.0% vs 101.6% [A], 103.2% vs 100.9% [B]).
Conclusions. Crushing the capsule contents did not impact the *in vitro* dissolution performance of valbenazine. Many patients with TD, particularly elderly patients, have difficulty swallowing and may benefit from alternative delivery methods for valbenazine, especially if other TD medications cannot be crushed. More research is needed to better understand if and how crushing the capsule contents of valbenazine affects their stability when mixed with food or delivered through a feeding tube.
Funding. Neurocrine Biosciences, Inc.

Digital CBT-I Treatment Improves Sleep and Reduces Anxiety and Depression Symptoms in Adults With Chronic Insomnia: Interim Analysis of DREAM Study

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Abstract

Introduction. Chronic insomnia (CI) often co-occurs with depression and anxiety, and treatment may positively impact mood. This ongoing study collected real-world data on changes in insomnia, depression, and anxiety symptoms among adults with CI treated with a prescription digital therapeutic (PDT) delivering cognitive-behavioral therapy for insomnia (CBT-I; Somryst®, previously SHUTi).
Methods. This prospective, single-arm, pragmatic clinical study enrolled adults (≥18 years) in the US with CI and mobile device access. The PDT consists of six core modules completed over

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6–9 weeks. In this interim analysis, participants completed the Insomnia Severity Index (ISI), 8-item Patient Health Questionnaire (PHQ-8), and Generalized Anxiety Disorder-7 scale (GAD-7) and other self-reported outcomes—at screening (baseline/prior to Core 1), end of treatment (Day 63), and 6-month follow-up (Day 243).

Results. Mean ISI scores decreased ($p<0.0001$) from baseline (n=991) to post-treatment (n=777;18.8 vs 11.3) and to Day 243 (n=193; 18.8 vs 12.1). Mean GAD-7 scores improved from baseline to Day 63 (n=744; $p<0.0001$, Cohen's $d = 0.48$) and to Day 243 (n=186; $p<0.0001$, $d = 0.45$). Similarly, PHQ-8 scores improved from baseline to Day 63 (n=747; $p<0.001$, $d = 0.76$) and to Day 243 (n=186; $p<0.0001$, $d = 0.60$). These patterns persisted across baseline anxiety and depressive severity levels among people with any baseline depressive or anxiety symptoms (all $p<0.05$ for depression, all $p<0.0001$ for anxiety), with large effect sizes observed for severe anxiety (d=1.43 Day 63, d=1.55 Day 243) and for moderate to severe depression (d range = 0.96-1.51).

Conclusion. In this study, treatment with digital CBT-I was associated with significant reductions in ISI, anxiety, and depression at posttreatment and at 6 months. The largest observed decreases in GAD-7 and PHQ-8 scores were among people with more severe baseline mood symptoms.

Funding. Pear Therapeutics (US), Inc.

Rates of Inpatient Hospitalizations Across a 2-Year Time Horizon Between reSET-O and Control Patients: A Difference in Differences Approach

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Abstract

Introduction. reSET-O® is an FDA-authorized prescription digital therapeutic (PDT) for opioid use disorder (OUD) providing cognitive behavioral therapy as an adjunct to buprenorphine therapy. This analysis describes differences in inpatient hospitalization rates over a 2-year period between patients treated with the PDT and those who were not.

Methods. A real-world claims analysis using the HealthVerity Private Source 20 database compared inpatient hospitalization rates (including intensive care unit stays and rehospitalizations) in patients who filled a reSET-O prescription ("cases") to patients not filling their prescription ("controls"). Index date was date of reSET-O initiation for cases, and prescription date for controls, from January 1, 2019 to June 30, 2020. Pre- and post-index incidence rates of HCRU were compared with the incidence rate ratio (IRR) using a repeated-measures negative binomial model, adjusted for age, sex, region, payer type, Charlson comorbidity index (CCI) score, and number of similar services in the 12 months pre-index with an offset for number of days in the 12-month post-index period. Adjusted differences in inpatient hospitalizations in cases vs. controls were evaluated at 3-month intervals beginning at 12 months pre-index through 12 months post-index, using a difference in differences (DID) approach.

Results. In this analysis, 901 cases (median age 36 years, 62.4% female, 73.9% Medicaid recipients, 95% treated with buprenorphine in the post-index period) were compared with 978 controls (median age 38 years, 55.1% female, 65.4% Medicaid recipients, 95% treated with buprenorphine in the post-index period). Incidence rate ratios of inpatient stays trended lower in later pre-post comparison periods among cases (IRRs 0.80, 0.95, 0.87, and 0.75 at 3-, 6-, 9-, and 12 months pre-post, respectively), and trended higher in later pre-post periods in controls (IRRs 0.93, 0.83, 0.86, 0.88 at 3-, 6-, 9-, and 12-month intervals respectively). The DID for controls vs. cases during the 12-month post interval compared to the 12-month pre-index rates, represented a 44% lower incidence of inpatient hospitalizations vs. controls between the first and last quarters of observation.

Conclusions. This difference in difference analysis showed a lower 12-month pre-post incidence rate ratio of inpatient hospitalizations for patients using reSET-O vs. controls, and a 24-month change in quarterly inpatient hospitalizations in reSET-O patients that was almost half that of controls.

Funding. Pear Therapeutics (US), Inc.

Reduced Healthcare Resource Utilization in Patients With Chronic Insomnia 24 Months After Treatment With Digital CBT-I: A Matched-Control Study

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Abstract

Introduction. This analysis examined the impact of a digital therapeutic for treating chronic insomnia (currently marketed as Somryst®, at the time called Sleep Healthy Using The internet [SHUTi]) on healthcare resource use (HCRU) by comparing patients treated with the digital cognitive behavioral therapy for insomnia (dCBTi) to patients not treated with dCBTi, but with insomnia medications.

Methods. A retrospective observational study using health claims data was conducted in two cohorts across the United States: patients who registered for dCBTi (cases) between June 1, 2016

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