Methods. Health insurance claims data from the IBM MarketScan Commercial Database and Multi-State Medicaid Database were analyzed. Individuals aged 18 to 64 with ≥1 inpatient or ≥2 outpatient claims for BD during the year preceding the analysis year (2015-2019) were included, with age- and sex-matched controls. Baseline demographic and clinical characteristics were evaluated. Opioid dispensing during each analysis year was defined as either chronic (coverage for ≥70 days in any 90-day period, or ≥6 prescriptions dispensed during analysis year) or nonchronic (≥1 prescription dispensed, not meeting chronic definition).
Results. BD patients had a higher prevalence of medical and psychiatric comorbidities, including pain diagnoses, vs controls. Among patients with BD in the Commercial database, chronic opioid dispensing decreased from 11% (controls: 3%) in 2015 to 6% (controls: 2%) in 2019, and in the Medicaid database, from 27% (controls: 12%) to 12% (controls: 5%). Among patients with BD in the Commercial database, nonchronic dispensing decreased from 26% (controls: 17%) in 2015 to 20% (controls: 12%) in 2019, and from 32% (controls: 26%) to 25% (controls: 14%) in the Medicaid database.
Conclusion. Between 2015 and 2019, there was a significant decrease in chronic and nonchronic prescription opioid dispensing among BD patients and controls across both the Commercial and Medicaid databases. Despite this finding, it is important to note that both chronic and nonchronic opioid dispensing was consistently higher for BD patients vs controls over time, across both databases.
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A Structured Benefit-Risk Assessment to Evaluate a Combination of Olanzapine and Samidorphan for the Treatment of Schizophrenia and Bipolar I Disorder

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Abstract

Background. A combination of olanzapine and samidorphan (OLZ/SAM) that provides the efficacy of olanzapine while mitigating weight gain was recently approved by the FDA for the treatment of schizophrenia and bipolar I disorder. To improve communication of the OLZ/SAM benefit-risk profile, a structured framework was utilized.

Methods. The Benefit-Risk Action Team framework was used to evaluate OLZ/SAM, with analyses completed for each pivotal study. ENLIGHTEN-1 evaluated antipsychotic efficacy and safety. ENLIGHTEN-2 evaluated the weight profile of OLZ/SAM vs olanzapine. Benefit-risk outcomes were selected based on study outcome parameters, known risks of olanzapine and samidorphan, and public health importance. A subset of opioid antagonist risks was not assessed due to clinical trial exclusions; however, they were factored into the overall evaluation. Risk differences and confidence intervals were analyzed.
Results. In ENLIGHTEN-1, OLZ/SAM had a lower risk of psychiatric discontinuation and nonresponse to treatment compared with placebo; higher risks of hyperprolactinemia, weight gain (≥7%), sedation, and worsening of fasting triglycerides and glucose, and no difference for fasting total and LDL cholesterol, neutropenia, orthostatic hypotension, and movement disorders. In ENLIGHTEN-2, OLZ/SAM had reduced risks of weight gain and waist circumference increase compared to olanzapine along with similar risks of relapse and psychiatric discontinuation and no difference in metabolic worsening, neutropenia, hyperprolactinemia, orthostatic hypotension, sedation, and movement disorders.
Discussion. Based on this assessment, OLZ/SAM has comparable efficacy and a safety profile consistent with olanzapine, with reduced weight gain. A structured approach to assessing the benefit-risk profile of a product facilitates transparent evaluation and communication.
Funding. Alkermes, Inc.

Development of the MIND-TD Questionnaire as a Screening Tool for Tardive Dyskinesia

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Abstract

Introduction. MIND-TD is a collaboration of healthcare professionals (HCPs) who are committed to raising awareness of tardive dyskinesia (TD), a persistent and potentially disabling movement disorder associated with prolonged exposure to antipsychotics and other dopamine receptor blocking agents. The MIND-TD questionnaire was developed to help HCPs screen for TD and facilitate discussion with patients.
Methods. In August 2020, an expert panel of 13 HCPs (4 psychiatrists, 6 neurologists/movement disorder specialists [MDSs], and 3 advanced practice providers [APPs]) met virtually to discuss potential screening questions for TD. This work was continued by

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4 panelists (1 psychiatrist, 2 neurologists/MDSs, and 1 APP) who tested the questions in clinical practice for revision and refinement. The same group also worked with the sponsor to develop 2 additional sections that could be used to elicit more information from patients. The panel recognized the need for a tool that could facilitate telehealth screening for TD, including audio-only interactions. Therefore, practices from speech-language pathologists (eg, diadochokinetics) were used to refine the questionnaire.
Results. Part 1 of the MIND-TD questionnaire includes a yes-or-no question for each of the 4 following topics: presence of extra or unwanted movements (Movement); feelings of embarrassment or self-consciousness (Impact); if anyone else has noticed the movements (Notice); and if movements interfere with everyday routines (Daily Activities). Part 1 can be administered by any trained medical staff, either in person or via telehealth (with video or audio-only). Routine administration is suggested in all patients who meet any of the following criteria: current or prior use of any first- or second-generation antipsychotic; use of an anticholinergic medication in conjunction with a current or past antipsychotic; or current diagnosis of TD. Part 2 of the MIND-TD questionnaire has 2 sections. The first (Thorough Interview) includes 9 items related to physical/functional difficulties (eg, eating, speaking, walking, and gripping objects) and 3 simple instructions for speech difficulties. The second section (Differentiate) includes checklists of characteristic movements for TD and drug-induced parkinsonism, along with an item related to akathisia and suggestions for observing abnormal or involuntary movements. Part 2 should be administered by the treating HCP in patients who have abnormal movements that may be related to TD. Part 2 requires visual observation of the patient, whether in-person or via video.
Conclusions. MIND-TD is a screening questionnaire that can facilitate a dialogue between HCPs and patients about the risks, symptoms, and impact of TD. The MIND questions can stand alone and be administered during in-person visits or telehealth visits (video or audio-only). The TD section can be used to gather more information about a patient's abnormal movements.
Funding. Neurocrine Biosciences, Inc.

Long-Term Effects of Once-Daily Valbenazine in Older and Younger Adults with Tardive Dyskinesia

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Abstract

Introduction. Older patients taking a dopamine receptor blocking agent (eg, first- or second-generation antipsychotic) have an increased risk for tardive dyskinesia (TD), a persistent and potentially disabling movement disorder. Valbenazine, a selective and potent vesicular monoamine transporter 2 inhibitor, is approved for once-daily treatment of TD with no dosing adjustments required for older patients. This analysis of valbenazine clinical trial data, which is the first to evaluate an approved TD medication in a population ≥65 years, was conducted to better understand treatment outcomes in older patients.
Methods. Data from two 48-week long-term studies (KINECT 3-extension, KINECT 4) were pooled and analyzed in older (≥65 years) and younger (<65 years) participants. Analyses based on the Abnormal Involuntary Movement Scale (AIMS) total score included: mean change from baseline (BL); clinically meaningful response (≥30% improvement from BL [AIMS-30%]); and protocol-defined response (≥50% improvement from BL [AIMS-50%]). Additional analyses included response thresholds for Clinical Global Improvement-Tardive Dyskinesia and Patient Global Impression of Change as follows: rating of "minimally improved" or better (score ≤3) at week 48 (CGI-TD≤3, PGIC≤3); rating of "much improved" or "very much improved" (score ≤2) at week 48 (CGI-TD≤2, PGIC≤2).
Results. AIMS outcomes in the older subgroup were generally comparable to (or better than) outcomes in the younger subgroup and overall study populations. In participants ≥65 years, pooled AIMS results indicated substantial improvements in TD movements with valbenazine 40 mg (n = 8) and 80 mg (n = 20): mean change from BL (−6.4 and −9.8 [for 40 and 80 mg, respectively]); AIMS-30% (75% and 95%); AIMS-50% (75% and 85%). CGI-TD and PGIC response rates indicated that clinician- and patient-reported global improvements were also substantial in the older subgroup: CGI-TD = 3 (88% and 100% [for 40 and 80 mg, respectively]); CGI-TD = 2 (88% and 95%); PGIC = 3 (88% and 100%); PGIC = 2 (75% and 90%).
Conclusions. These analyses, which are the first to evaluate long-term valbenazine effects in patients ≥65 years, indicate that older study participants had clinically meaningful and substantial improvements in TD that were comparable to (or better than) those in younger participants.
Funding. Neurocrine Biosciences, Inc.

Rhabdomyolysis in Young Adult Male Stabilized on Mirtazapine and with History of COVID-19 Infection

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Abstract

Study Objective. The purpose of this case study is to review the clinical presentation and medical workup of a young adult male presenting with rhabdomyolysis in the setting of suspected contributing factors, including treatment with mirtazapine and history of COVID-19 infection.
Method. This case study involves a 19-year-old male in a residential setting with a psychiatric history of major depressive disorder and post-traumatic stress disorder who had been stabilized on mirtazapine for 9 months. Then, the patient exhibited fever, sore throat, cough, nausea, diarrhea, and malaise and was

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