Prescription digital therapeutics (PDTs) are FDA-authorized treatments delivered via mobile devices (eg, smartphones). A real-world pilot study was conducted in an outpatient addiction treatment program to evaluate patient engagement and use of a PDT for patients with OUD. The objective was to assess the ability of the PDT to improve engagement and care for patients receiving buprenorphine medication for opioid use disorder (MOUD).
Methods. Patients with OUD treated at an ambulatory addiction treatment clinic were invited to participate in the pilot. The reSET-O PDT is comprised of 31 core therapy lessons plus 36 supplementary lessons, plus contingency management rewards. Patients were asked to complete at least 4 lessons per week, for 12-weeks. Engagement and use data were collected via the PDT and rates of emergency room data were obtained from patient medical records. Data were compared to a similar group of 158 OUD patients treated at the same clinic who did not use the PDT. Abstinence data were obtained from deidentified medical records.
Results. Pilot participants (N = 40) completed a median of 24 lessons: 73.2% completed at least 8 lessons and 42.5% completed all 31 core lessons. Pilot participants had significantly higher rates of abstinence from opioids in the 30 days prior to discharge from the program than the comparison group: 77.5% vs 51.9% ($P < .01$). Clinician-reported treatment retention for pilot participants vs the comparison group was 100% vs 70.9% 30 days after treatment initiation ($P < .01$), 87.5% vs 55.1% at 90 days post-initiation ($P < .01$), and 45.0% vs 38.6% at 180 days post-initiation ($P = .46$). Emergency room visits within 90 days of discharge from the addiction program were significantly reduced in pilot participants compared to the comparison group (17.3% vs 31.7%, $P < .01$).
Conclusions. These results demonstrate substantial engagement with a PDT in a real-world population of patients with OUD being treated with buprenorphine. Abstinence and retention outcomes were high compared to patients not using the PDT. These results demonstrate the potential value of PDTs to improve outcomes among patients with OUD, a population for which a significant need for improved treatments exists.
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A Model-Informed Drug Development Approach Supporting the Approval of a New Valbenazine Dose for Tardive Dyskinesia

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Abstract

Introduction. Tardive dyskinesia (TD) is a persistent and potentially disabling movement disorder associated with dopamine receptor blocking agents (eg, antipsychotics). Valbenazine is a highly selective vesicular monoamine transporter 2 inhibitor with several safe and effective dosing options now approved for once-daily (QD) treatment of TD in adults. Valbenazine 80 mg QD is the recommended dose for TD; however, 40 or 60 mg QD (newly approved dose) may be considered depending on response and tolerability. The recent approval of valbenazine 60 mg was based on results from an analysis that used the FDA's model-informed drug development (MIDD) approach and leveraged existing data from the 6-week, phase 3 registration trial of valbenazine (KINECT 3).
Methods. A population pharmacokinetic (popPK) model was developed to describe plasma concentration-time profiles for valbenazine and its primary active metabolite, [+]-α-dihydrotetrabenazine ([+]-α-HTBZ). An exposure-response (E-R) model was developed using the area under the concentration-time curve (AUC) of [+]-α-HTBZ (exposure) and change from baseline in the Abnormal Involuntary Movement Scale total score (AIMS-CFB) (response). Stepwise E-R model development evaluated various linear and nonlinear models to describe AIMS-CFB vs [+]-α-HTBZ AUC and time. E-R relationships established with the 40 and 80 mg data were used to predict AIMS-CFB for a 60 mg dose up to week 6, accounting for study-to-study, inter-individual, and residual variabilities.
Results. Steady-state valbenazine and [+]-α-HTBZ concentrations were well described by a joint parent-metabolite popPK model. An Emax model with asymptotic exponential delay in the maximal valbenazine effect adequately characterized the E-R relationship between AIMS-CFB and [+]-α-HTBZ AUC. The simulated confidence intervals of response were consistent with the observed KINECT 3 results, demonstrating the utility of the model to predict efficacy results. The established E-R model was subsequently used to predict AIMS-CFB for valbenazine 60 mg QD at week 6. Mean AIMS scores decreased (improved) in a dose-dependent manner, with 60 mg QD predicted to result in least-squares mean (SEM) AIMS-CFB of −2.7 0.4, which is between the reported AIMS-CFB for 40 mg (−1.9 ± 0.4) and 80 mg (−3.2 ± 0.4). All simulated trials demonstrated valbenazine 60 mg to be significantly superior to placebo in AIMS-CFB after 6 weeks of treatment.
Conclusions. This analysis integrated and leveraged data from two previously approved valbenazine doses (40 and 80 mg QD) using an MIDD approach. The results provided key evidence that an intermediate dose (newly approved 60 mg QD) could be considered therapeutically beneficial without the need for an additional clinical trial. The availability of a valbenazine 60 mg dose to complement the previously approved doses fills an existing medical need for patients with TD who could benefit from this third effective dose.
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