trials, lumateperone improved symptoms of schizophrenia with the same trajectory and same magnitude of improvement from baseline to endpoint on the PANSS total score.
Lumateperone was well-tolerated with a favorable safety profile in all studies. In the two studies with risperidone included as an active control, lumateperone was statistically significantly better than risperidone on key safety and tolerability measures. In the open-label safety switching study statistically significant improvements from SOC were observed in body weight, cardiometabolic and endocrine parameters worsened again when switched back to SOC medication. In this study, symptoms of schizophrenia generally remained stable or improved. Greater improvements were observed in subgroups of patients with elevated symptomatology (comorbid symptoms of depression and those with prominent negative symptoms).

DISCUSSION: Lumateperone represents a novel approach to the treatment of schizophrenia with a favorable safety profile in clinical trials. The lack of cardiometabolic and motor safety issues presents a safety profile differentiated from standard-of-care antipsychotic therapy.
Funding Acknowledgements: Intra-Cellular Therapies, Inc.

31
A Modified-Release Drug Delivery Technology Containing Amphetamine-Ion Exchange Complexes

Barry K. Herman, MD, MMM[1]; Thomas R. King, MS, MPH[1]; Judith C. Kando, PharmD; BCPP[1]; and Antonio Pardo, MD[1]

[1] Tris Pharma, Inc., Monmouth Junction, NJ

ABSTRACT: The proprietary, immediate and extended drug delivery technologyLiquiXR® utilizes an ion-exchange resin that complexes with amphetamine or any active moiety that can be protonated and is water-soluble. The active ingredient of the drug product forms a complex with an ion exchange polymer of the resin resulting in micron-sized particles. A portion of these particles is then coated with an aqueous, pH-independent polymer designed to provide sustained release of drug product. The polymer coating applied to the ion-exchange resin particles is of varying thickness, allowing for extended release of active drug while uncoated particles provide for immediate release of drug.
The micron-sized particles lend themselves to being formulated into an appropriate dosage form: solid/chewable tablet, liquid suspension, orally disintegrating tablet, film, or capsules. Active ingredient of drug product is subsequently released from the dosage form in millions of particles, with release driven by a combination of ion exchange and diffusion. After drug release, the ion-exchange resin particles are excreted in the feces.
The release characteristics of LiquiXR allow for customized, sustained release of active drug ~24 hours post dose. Mechanistically, drug particles enter the gastrointestinal (GI) tract. As positively-charged ions from GI fluids diffuse across the coating, it displaces drug ions from product and they diffuse through the coating and into the GI fluids for absorption. As the coating is of variable thickness, some drug product takes longer to diffuse and absorb, providing for the delayed drug release characteristics.
The LiquiXR drug delivery technology has already been successfully utilized in the development of treatment options (liquid suspension and chewable tablet) that offer rapid absorption and sustained plasma levels after once-daily dosing. LiquiXR is utilized in Dyanavel® XR (amphetamine extended-release oral suspension; AMPH EROS), which is indicated for treatment of ADHD. It comprises 2.5 mg/mL amphetamine base and uses LiquiXR technology to provide an immediate release component followed by an extended-release profile.
Efficacy of AMPH EROS was established in children 6 to 12 yr in a Phase 3, placebo-controlled laboratory classroom study. In that study, ADHD symptoms in children on an individually optimized dose of amphetamine (range 10–20 mg/day) were statistically significantly improved compared with symptoms in children treated with placebo. For children treated with AMPH EROS, onset of effect was demonstrated at 1 hour after dosing, and efficacy was observed through 13 hr post-dose. The effect size (ES) was comparable to ES demonstrated for other psychostimulants tested in studies using a similar design. The efficacy data reported for AMPH EROS provides an excellent example of the potential utility and clinical application for other active drug products requiring an immediate and extended release profile.
Funding Acknowledgements: Support provided by Tris Pharma, Inc.

32
Early-Onset Efficacy and Safety Pilot Study of Amphetamine Extended-Release Oral Suspension (AMPH EROS) in the Treatment of Children with Attention-Deficit/Hyperactivity Disorder

Ann C. Childress, MD[1]; Antonio Pardo, MD[2]; Thomas R. King, MS, MPH[2]; Judith C. Kando, PharmD, BCPP[2]; and Barry K. Herman, MD, MMM[2]

[1] Center for Psychiatry and Behavioral Medicine, Inc. Las Vegas, NV
[2] Tris Pharma, Inc., Monmouth Junction, NJ

https://doi.org/10.1017/S1092852919000269 Published online by Cambridge University Press

OBJECTIVE: To determine whether amphetamine extended-release oralsuspension (AMPH EROS) has an onset of effect at 30 minutes postdose inchildren with ADHD.

METHODS: This randomized, double-blind, 2-treatment, 2-sequence, placebo-controlled crossover pilot study enrolled subjects aged 6 to 12 years withattention-deficit/hyperactivity disorder (ADHD) and ADHD-Rating Scale-5 scores of ≥90th percentile for sex and age. A dose of 5 to 20 mg/day of AMPH EROS was determined during a 1-week open-label phase based on medication history, symptom control, and tolerability. Subjects completed a practice laboratory classroom then received one day of double-blind active drug or placebo each in random sequence during 2 double-blind laboratory classroom days. Subjects completed the first double-blind laboratory classroom session, returned to open label drug for 5 days then crossed over on day 6 during a second double-blind laboratory classroom session. DB dose was fixed at AMPH EROS 15, 17.5, or 20 mg . The primary endpoint was change from predose in the Swanson, Kotkin, Agler, M-Flynn, Pelham rating scale-combined score (SKAMP-C) at 30 minutes postdose on two DB days. The key secondary endpoint was change from predose in the SKAMP-C score at 3 hours postdose for AMPH EROS compared with placebo. Safety assessments included vital signs and adverse events.

RESULTS: Eighteen subjects were enrolled in the study (14 males and 4 females) with a mean age of 9 years. At both 30 minutes and 3 hours postdose, changes from baseline in SKAMP-C for AMPH EROS vs. placebo were statistically significant ($p < 0.01$ and $p = 0.0002$, respectively) with corresponding effect sizes of 0.96 and 1.57. Adverse events (>10%) during the open-label phase included upper respiratory tract infection, fatigue, upper abdominal pain, headache, decreased appetite, and affect lability.

CONCLUSIONS: AMPH EROS was effective in reducing ADHD symptoms at 30 minutes postdose. AEs were mild or moderate and consistent with those of other extended-release amphetamines.

Funding Acknowledgements: Support was provided by Tris Pharma, Inc.

33
An Intervention to Decrease Benzodiazepine Prescribing by Providers in an Urban Clinic

Lois Platt, DNP, PMHNP-BC, LCPC[1]; Teresa A. Savage, PhD, RN[2]; and Nimmi Rajagopal, MD, FAAFP[3]

[1] Clinical Instructor, University of Illinois, Chicago, IL (presenter)
[2] Associate Professor, University of Illinois, Chicago, IL
[3] Assistant Professor of Clinical Family Medicine, University of Illinois, Chicago, IL

ABSTRACT: STUDY OBJECTIVES: Outpatient benzodiazepine use can cause side effects including dependence (20–30%) and death from respiratory depression when used with alcohol or opioids. Benzodiazepine use is on the rise in the U.S., increasing 67% from 1996–2013. In this quality improvement project, two educational interventions were combined with the intent of decreasing benzodiazepine prescribing by providers (MDs, APRNs) in an urban university clinic.

STUDY QUESTION: When prescribers working in a low-income clinic receive an intervention to increase awareness of benzodiazepine dangers and promote harm reduction strategies compared to treatment as usual, do they write fewer benzodiazepine prescriptions in the month following the intervention?

METHOD: A hybrid intervention combining academic detailing (educational outreach visits) and pharmaceutical industry detailing (merchandising, relationship building) was provided in two sessions to family practice providers (salaried and residents) working in a university outpatient clinic in Chicago. The subject matter included benzodiazepine risks, alternative treatments for anxiety & insomnia, and methods to deal with patient demand. All clinic providers (n = 40) were invited to participate. Participants were self-selected to attend each session (although resident physicians were obligated to attend). A total of 20–24 providers attended each session.
Benzodiazepine prescription information was extracted by clinic information systems for two periods: 12 months pre-intervention, and 30 days post-intervention. For ease of comparison, each prescription was converted to a common denominator: the diazepam-equivalent dose. The pre-intervention monthly average (for one year) was compared to 30-day post-intervention data. The outcome measure was the numeric difference in the prescribed diazepam-equivalents pre- and post-intervention. This number was used as a measure of the effectiveness of the intervention. A decrease in prescribing post- compared to pre-intervention would indicate a successful intervention.

RESULTS: There was an 80% decrease in benzodiazepine prescribing in the 30-day post-intervention period compared to the 12-month pre-intervention monthly average. This result cannot be explained by personnel changes at the clinic. Although these did occur in 2017, the pattern of prescribing was stable throughout the year prior to this intervention.

CONCLUSIONS: The combination of academic and pharmaceutical industry detailing influenced family practice

https://doi.org/10.1017/S1092852919000269 Published online by Cambridge University Press