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ABSTRACT: Objective: Tardive dyskinesia (TD) is a hyperkinetic movement disorder associated with antipsychotic treatment. RE KINECT (NCT03062033), a real-world study of outpatients prescribed antipsychotics, was designed to identify the presence of possible TD and characterize the impact of involuntary movements on functioning and quality of life. Data from RE-KINECT were used to compare the impact of possible TD in patients with schizophrenia/schizoaffective disorder [SZD] versus mood/other psychiatric disorders [Mood].

METHODS: Adults with ≥3 months of lifetime exposure to antipsychotics and ≥1 psychiatric disorder were recruited. The presence of possible TD was based on clinicians' observation of involuntary movements in 4 body regions (head, trunk, upper extremities, and lower extremities). Baseline outcomes included demographics, medication history, location/severity of abnormal movements, impact of abnormal movements on daily activities, the Sheehan Disability Scale (SDS), and the EuroQoL 5-Dimensional questionnaire (EQ-5D-5L).

RESULTS: Of 204 patients with clinician-confirmed possible TD, 111 (54.4%) had a SZD diagnosis and 93 (45.6%) had a mood/other psychiatric diagnosis. Significant differences found between groups (Mood vs SZD) included: mean age (56.9 vs 52.7 years; $P = 0.0263$); male sex (33.3% vs 62.2%; $P < 0.0001$); African-American race (7.5% vs 26.1%; $P = 0.0005$); mean lifetime exposure to antipsychotics (9.5 vs 19.5 years; $P < 0.0001$); and percentage of patients currently taking ≥2 psychiatric medications (93.5% vs 79.3%; $P = 0.0093$). Based on clinician observation, there were no significant differences between diagnosis groups in the number of body regions impacted by abnormal movements, maximum severity score across all 4 regions, or patient awareness of possible TD. Over 30% of patients in both groups reported that involuntary movements had "some" or "a lot" of impact on their ability to continue usual activities, be productive, and socialize. No significant differences between the diagnosis groups (Mood vs SZD) were found for mean SDS total score (12.8 vs 10.8), SDS domain scores (work/school [4.1 vs 4.2], social life [4.3 vs 3.7], family life [4.1 vs 3.5]), EQ-5D-5L utility score (0.68 vs 0.74), or EQ-5D-5L health state VAS (64.8 vs 68.5).

CONCLUSIONS: In this cohort of outpatients with possible TD, those with Mood disorders were more likely to be older, female, and white than patients with SZD. The ability to function and quality of life were equally impaired in both groups. Further studies on the impact of TD are needed.
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Phase 3 Randomized, Double-blind, Placebo-Controlled Studies Evaluating Efficacy and Safety of Extended-Release Viloxazine for Pediatric ADHD

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ABSTRACT: Study Objectives: Although stimulants are commonly used for attention-deficit/hyperactivity disorder (ADHD), 10–30% of patients have an inadequate response, adverse events, or comorbidities preventing use. Thus, there is a need for safe, effective nonstimulant options. Extended-release viloxazine (SPN-812), a nonstimulant, is currently in development for the treatment of ADHD in children and adolescents. SPN-812 is a structurally distinct, bicyclic norepinephrine reuptake inhibitor with selective serotonergic activity. Results of the Phase 2 program demonstrated efficacy (improved mean ADHD Rating Scale-IV total score) and safety of SPN-812 in children (6–12 years), as well as an onset of action within 1–2 weeks.

METHOD: Four ongoing Phase 3 randomized, double-blind, placebo-controlled, outpatient, US studies are investigating the efficacy and safety of once-daily SPN-812 for ADHD in children (ages 6–11; 100–400 mg) and adolescents (ages 12–17; 200–600 mg). Two studies are enrolling children and two are enrolling adolescents. Eligible subjects are required to have minimum baseline scores of ≥28 for ADHD-RS-5 and ≥4 for Clinical Global Impression-Severity scale (CGI-S). These studies will randomize ~1200 subjects, with ~800 subjects receiving SPN-812 over a 1–3-week titration and 5-week

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maintenance period. The primary endpoint in all studies is mean change from baseline to end of study (EOS) in ADHD-RS-5 total score for SPN-812 vs. placebo. Secondary endpoints include change from baseline to EOS in 30% responder rate (% change: ADHD RS 5); Hyperactivity/Impulsivity and Inattention ADHD-RS-5 subscale scores; Conners 3 Rating Scale (parent and self-report); CGI-S/CGI-I (Improvement); Weiss Functional Impairment Rating Scale (parent report); Parenting Stress Index (children); and Stress Index for Parents of Adolescents (adolescents) after 6–8 weeks of treatment. Safety is assessed via adverse events, clinical laboratory tests, vital signs, electrocardiograms, physical examinations, and the Columbia-Suicide Severity Rating Scale. Phase 3 completers are offered the option of enrolling in an open-label extension study (OLE; up to 3 years) with a starting dose of 100/200 mg (children/adolescents). Data will be summarized with descriptive statistics and analyzed using appropriate statistical methods.

RESULTS: As of August 2018, enrollment in 1 child study is complete, and the other 3 trials are at ~89%; rollover into the OLE is ~90%.

CONCLUSIONS: There is an unmet need for nonstimulant ADHD treatment for children and adolescents that is effective, long-acting, and well tolerated. SPN-812 is being investigated in four Phase 3 randomized, placebo-controlled studies for the treatment of children and adolescents with ADHD, based on demonstrated efficacy and safety in the Phase 2 program.

This study is an encore of a poster presentation at the 2018 Annual Meeting of the American Society of Clinical Psychopharmacology (ASCP).

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Pharmacodynamics and Tolerability of Intranasally Administered Immediate-Release Amphetamine Sulfate Among Recreational Intranasal Stimulant Users

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ABSTRACT: Study Objective: Despite increased nonmedical use of ADHD prescription stimulants, there are limited data to inform selection of intranasal doses for abuse-potential evaluations. This study determined a dose of amphetamine sulfate that is tolerable and distinguishable from placebo on pharmacodynamic (PD) measures.

METHODS: In this randomized, double-blind, placebo-controlled, dose-escalation study, healthy, nondependent, recreational stimulant users received a single intranasal dose of amphetamine sulfate (20, 30, or 40 mg ; n = 6 per group) or placebo (n = 2 per group). PD and safety were assessed pre-dose and ≤24 hours post-dose. Drug Liking was measured using a bipolar Visual Analogue Scale (VAS; 0–100). Dose selection criteria were complete dose insufflation (≥95%); demonstration of peak Drug Liking ≥75 points, and ≥15 points greater than placebo in ≥3 participants receiving active drug; and tolerability.

RESULTS: Peak Drug Liking criteria were met in the 20-, 30-, and 40-mg groups by 2, 0, and 6 participants, respectively. Mean (SD) peak Drug Liking was 62 (13.0), 71 (17.8), and 93 (8.7) for amphetamine sulfate versus 54 (3.5), 76 (34.6), and 51 (0) for placebo in the 20-, 30-, and 40-mg groups, respectively. Thirteen participants experienced mild AEs (n = 1, 4, 6, and 1 in 20-, 30-, 40-mg, and placebo groups, respectively), there were no serious or clinically significant AEs. The most common AE was nostril burning sensation (active drug, n = 7). There were no instances of an incompletely insufflated dose.

CONCLUSION: A 40-mg intranasal dose produced distinguishable PD effects and was well tolerated. This dose has been selected for further abuse-potential evaluations.

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Therapeutic Equivalences in Long-term Antipsychotics

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ABSTRACT: Study Objectives: The concept of dose equivalence is very useful when it comes to using drugs. In the case of antipsychotics, the first comparison was