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

established by Davis in 1974, called the classical comparison method. Subsequently, other methods have appeared, such as the minimum effective dose method, the dose response method, the consensus among experts such as consensus method by Gardner, and the Daily Dose method of the World Health Organization. In 2016, Leucht et al performed the meta-analysis comparing the equivalence by the alternative methods of second-generation antipsychotics orally, based on Olanzapine. However, therapeutic equivalences between injectable antipsychotics have not yet been made.
The objective of the study is to establish a pattern of therapeutic equivalences between long-acting antipsychotics, based on the method of the Defined Daily Dose (DDD).

METHOD: The DDD is the dose of the maintenance medium of a drug for its main indication in adults of 70 kg. In the case of antipsychotics, psychosis is the most important indication. DDDs are different for each route of administration, especially if the bioavailability of the drug varies between one route and another. To establish the DDD of a drug, 3 measures are taken: firstly, the dose ranges of the drug approved by at least 1 major regulatory authority. Secondly, doses used in clinical trials. Thirdly, post marketing data on dose used in clinical practice when the drug is commercialized. Depot formulations are usually assigned the same DDDs as the ordinary oral dosage form. Based on the DDD according to the WHO classification at http://www.whocc.no/.
For comparison, Olanzapine 210 mg was used as the main drug and equivalences were established from it. Therapeutic deposit of Aripiprazole (ARI), Flufenazine decanoate (FLU), Haloperidol Decanoate (HAL) Olanzapine pamoate (OLA), Paliperidone palmitate (PAL), Risperidone depot (RIS), and Zuclopenthixol decanoate (ZUC).

RESULTS: The results will be shown in a 8x8 table.

CONCLUSIONS: DDD is available for almost all antipsychotics and is an accepted method as well as a clinical level as a researcher. They are based on a wide variety of data from different sources. Several studies have found a strong correlation between this method and other methods of equivalence. This method also has limitations. First, the DDDs were not established for the purpose of therapeutic equivalences. Secondly, the daily dose can be applied mainly to the efficacy of the drug, when the dose could cause some adverse effects.
The establishment of therapeutic equivalences may help when a clinician needs to change one long-term antipsychotic. This could reduce psychotic relapses. It may enhance therapeutic adherence avoiding undesirable side effects. On the other hand, long-acting antipsychotics have corroborated the adherence and decrease of relapses, which is why it is increasingly used as a good alternative to oral drugs.

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Impact of Aripiprazole Long-acting Injectable (ALAI) Initiation on Hospitalizations and Visits to Emergency

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ABSTRACT: Background: Aripiprazole once-monthly is an LAI formulation of aripiprazole that is currently approved in the USA and Europe for the treatment of schizophrenia. Some studies have reported a decline in hospital admissions and emergency use after initiation on long-acting injectable (LAI) antipsychotics, but the effects of using recently commercialised LAI aripiprazole remains uncertain.

AIMS: To characterize the impact of ALAI initiation on number of hospitalizations and visits to the emergency service, among patients suffering from schizophrenia attending regularly to psychiatric consultations of Gregorio Marañón University General Hospital (Madrid, Spain).

METHODS: Patients initiated on (ALAI) were studied in an observational mirror-image design to assess changes in number of hospitalizations and visits to the emergency service in the 12 months pre- vs 12 months post-depot initiation. Other sociodemographic, physical and clinical variables such as age, gender, weight, blood pressure and presence of dual disorders were also gathered. Variables were collected reviewing clinical records.
Wilcoxon test was used to assess hospitalizations and visits to the emergency. Paired t-tests were used to assess changes in weight and blood pressure. Non parametric Mann-Whitney U test was used to compare aripiprazole doses between genders and in order to assess de influence of dual disorders. In order to perform the statistical analysis, IBM SPSS statistics v.20 was used.

RESULTS: 31 patients were included in the final analysis. Mean age was 44.67 (SD = 15.57) years. Most of the patients were male (54.8% vs 45.2%). 71% were previously receiving oral antipsychotics treatment, whereas 29% were receiving other LAI antipsychotic: no significant differences were observed when comparing hospitalizations ($p = 0.74$) or emergency use ($p = 0.98$) in the 12 months post-initiation

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