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Methods: Metabolic and cardiovascular data from 357 chronically ill (38.3 + 10.05 years old, 251 Male, 70.4% African-American) schizophrenia patients who were screened for participation in clinical trials from 1998-2007 (80.2% on atypical antipsychotics, 12.3% on typical antipsychotics, 7.5% untreated) were compared to a sample of 2,531 non-schizophrenic age-matched controls from the 2003-2004 Center for Disease Control and Prevention's **National Health and Nutrition Examination Survey** (NHANES) on measures including fasting blood sugars and lipids, BMI, and blood pressure.
Results: 29.1% of patients were overweight (BMI>25) and 37.8% were obese (BMI>30). Fasting lipids, cholesterol and triglycerides were elevated in 39.3% and 40.5% of patients respectively. Elevations in fasting blood sugar (FBS >110mg/dl) were found in 16.7% of patients with 7.6% having diabetes (FBS >126mg/dl). 15.5% were hypertensive (diastolic BP >85mmHg), and 54.5% had abnormal ECGs. 34% had metabolic syndrome (n=189). There were no differences across variables when compared to the age-matched NHANES controls. No association with either typical or atypical neuroleptic treatment was found based on χ^2 tests of differences.
Conclusions: Lack of differences with recent NHANES control data and lack of association with neuroleptic therapy suggests that other factors besides neuroleptic treatment (eg. diet, lifestyle) play a role in metabolic and cardiovascular abnormalities found in schizophrenia patients.

908. Efficacy and Tolerability of Paliperidone Palmitate: 9-week, Placebo-Controlled Study in Schizophrenia Patients

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Background: This study evaluated the efficacy and safety of paliperidone palmitate, a long-acting injectable agent, in the treatment of schizophrenia patients.
Methods: A 9-week, double-blind, placebo-controlled study randomized patients to placebo or paliperidone palmitate 50 or 100 mg eq. on Days 1, 8 and 36 (without oral supplementation). Efficacy and tolerability were evaluated via changes in mean Positive and Negative Syndrome Scale (PANSS) total scores and adverse event (AE) reporting, respectively.
Results: The intention-to-treat population included 197 patients (male=62%, mean±standard deviation [SD] age=39.3±10.3y; placebo N=66; paliperidone palmitate 50 mg eq. N=63; paliperidone palmitate 100 mg eq. N=68). Mean±SD PANSS total scores significantly improved ($p \leq 0.001$) from baseline (87.0±12.5) to end point for paliperidone palmitate 50 mg eq. (–5.2±21.5) and 100 mg eq. (–7.8±19.4) versus placebo (+6.2±18.3), with significant improvements observed from Day 8. Responder rates (≥30% improvement in PANSS total score at end point) were significantly greater in both paliperidone palmitate groups versus placebo ($p \leq 0.007$). AEs occurring ≥3% more in either paliperidone palmitate group versus placebo (safety population, N=247) were insomnia, schizophrenia, restlessness, sedation, extrapyramidal disorder, hypertonia, attention disturbance, electrocardiogram abnormal, constipation, myalgia, asthenia and vertigo. Extrapyramidal symptoms–AE rates were comparable for paliperidone palmitate and placebo, with the exception of parkinsonism (7% and 1%, respectively). Serious AEs in ≥1 patient (any group) were schizophrenia and psychotic disorder. Injections were generally well tolerated. No deaths occurred.
Conclusions: Paliperidone palmitate (50 and 100 mg eq. doses) is effective and well tolerated in acute symptomatic schizophrenia.
Supported by Johnson & Johnson Pharmaceutical Services, LLC., and Johnson & Johnson Pharmaceutical Research & Development

909. Pharmacokinetics (PK) of Multiple Doses of Olanzapine Long Acting Injection (OLAI), an Intramuscular (IM) Depot Formulation of Olanzapine (OLZ), in Stabilized Patients with Schizophrenia

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Background: Olanzapine pamoate is a long-acting depot formulation of OLZ that is an effective treatment for patients who benefit from the advantages of a depot. It has not yet been approved.
Methods: Schizophrenic patients stabilized on daily oral OLZ received multiple OLAI injections at doses of 100, 150, 160, 200, and 300 mg/2 weeks and 200, 255, 300, and 405 mg/4 weeks for 24 weeks. After each injection, serial plasma OLZ concentration samples were collected. PK were characterized using non-compartmental methods.
Results: The injections were well tolerated overall. Absorption-limited PK were observed. Plasma OLZ concentrations were sustained throughout both the 2- and 4-week injection intervals. On average, OLZ concentrations accumulate 2- to 3-fold upon multiple dosing and reach steady-state conditions after about 3 months of dosing. Peak-to-trough fluctuation in OLZ concentrations averages 51% for the 2-week injection interval and 75% for the 4-week interval. Maximum concentration and area under the concentration versus time curve for OLZ were proportionate to OLAI dose. Relative to oral OLZ (t_{max} = 6 hr, $t_{1/2}$ = 29 hr), the time of peak concentration following OLAI was 4 days and the half-life was approximately 26 days. The average steady-state concentrations sustained by OLAI correspond to those maintained by daily OLZ in the dosage range of 5-20 mg/day.
Conclusions: IM administration of OLAI is well tolerated and provides steady-state concentrations that are sustained over 4 weeks and are comparable to oral treatment.
Supported by Eli Lilly and Company

910. Relapse Prevention: Risperidone Long-Acting Injectable Vs Quetiapine or Aripiprazole

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Background: To investigate if risperidone long-acting injectable (RLAI) provides better efficacy maintenance over 2 years, as measured by the time to relapse, in comparison to the oral atypical antipsychotic quetiapine or aripiprazole.
Methods: Open-label, active-controlled, multicenter, randomized, 2-year trial of RLAI versus oral quetiapine or aripiprazole in 731 patients with schizophrenia currently treated with oral risperidone, olanzapine or conventional neuroleptics. Symptomatically stable patients on a stable dose of an antipsychotic for ≥4 weeks were enrolled. Primary efficacy evaluation was time to relapse. Secondary efficacy evaluations included: Positive and Negative Syndrome Scale (PANSS), Clinical Global Impression-Severity (CGI-S), Montgomery-Asberg Depression Rating Scale (MADRS) and Social and Occupational Functioning Assessment Scale (SOFAS). Safety evaluations included adverse events monitoring, Extrapyramidal Symptom Rating Scale (ESRS), clinical laboratory tests and vital signs.
Results: 808 subjects were screened and 731 (58.3% male, mean age 41.5 [SD:12.8] years) were randomised to treatment. Mean time since first onset was 13.9 (SD:11.2) years; mean time since first treatment was 12.5 (SD:10.7) years. At baseline 34.4% of subjects fulfilled the remission severity criteria. Reasons for switching (>1 allowed) included: insufficient efficacy; negative (29.8%), positive (14.1%), and general symptoms (21.1%) and adverse events (18.9%). Baseline scores were: PANSS: 73.0 (SD:21.8), CGI-S: 3.7 (SD:1.0),