Schizophrenia Research
Volume 98, Supplement, February 2008, Pages 165-166

322 – Efficacy/tolerability of paliperidone palmitate: 9-week, placebo-controlled study in schizophrenia patients

M. Kramer [1], R. Litman [2], R. Lane [3], M. Kujawa [1], P. Lim [1], D. Hough [1], M. Eerdekens [4]

320 – IMPROVEMENTS IN EVERYDAY FUNCTIONING WITH ATYPICAL ANTIPSYCHOTIC TREATMENT: A RANDOMIZED LONG-TERM COMPARISON OF ZIPRASIDONE AND HALOPERIDOL

P. Harvey[2], **C. Kremer**[1], I. Lombardo[1].

[1]*Pfizer Inc., 235 East 42nd Street, New York, NY 10017 USA*
[2]*Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Woodruff Memorial Building, 101 Woodruff Circle, Suite 4000, Atlanta, GA 30032 USA*

Presenting Author details: charlotte.m.kremer@pfizer.com
235 East 42nd St, NY 10016 New York, United States,
Tel.: +1 212 733 0140; fax: +1 646 441 4614.

Background: Several studies have examined the development of clinical remission during treatment of schizophrenia. However, development of remission may not be associated with functional recovery, which must be examined separately. This study examined the development of "functional remission" in a long-term double-blind comparison of haloperidol and ziprasidone.
Methods: Community dwelling patients with schizophrenia were randomized to treatment with haloperidol ($n=47$) or ziprasidone dosed either once or twice daily ($n=139$) and re-examined at follow-up intervals ranging up to 196 weeks. Their community functioning was examined with the Heinrichs–Carpenter Quality of Life Scale. Both total scores for employment and social functioning and achievement of improvement milestones across the individual items were analyzed.
Results: Mixed random effects models adjusting for length of follow-up indicated a significant ($p<.05$) treatment effect favoring ziprasidone for social functioning. While the mixed model was not significant for employment, the 95% confidence interval for changes scores in the haloperidol group overlapped with 0, while mean change was significantly greater than 0 for the ziprasidone group. Most importantly, the distributions of change scores across the items showed significantly more items where endpoint scores were 5 or 6 (minimal to no impairment) in ziprasidone treated patients, ($X^2[8]=16.92$, $p=.03$). There was an overall shift in the distribution of endpoint scores, with haloperidol patients having fewer items where substantial change was detected than ziprasidone patients.
Conclusions: Treatment with ziprasidone was associated with greater functional gains than treatment with haloperidol, even when differential dropout was controlled. Both treatment retention and functional gains favored ziprasidone in this long-term study.

doi:10.1016/j.schres.2007.12.387

321 – COMPARISON OF POST-MARKETING SPONTANEOUSLY REPORTED ADVERSE EVENTS IN OLANZAPINE-TREATED ADOLESCENT AND ADULT PATIENTS

L. Kryzhanovskaya[1], D. Falk[1], L.M. Schuh[1], J. Wernicke[1].

[1]*Lilly Research Laboratories, Indianapolis, USA*

Presenting Author details: zyp_sci_comm@lilly.com
Lilly Corporate Center, 46285 Indianapolis, United States,
Tel.: +1 317 651 2802; fax: +1 317 433 0448.

Background: Atypical antipsychotic agents are increasingly prescribed for adolescent patients, but most, including olanzapine, are not approved for them. Relatively little information is available comparing spontaneously reported post-marketing adverse events in adolescents and adults.
Methods: Spontaneous serious and nonserious adverse event reports from postmarketing experience in the Lilly Safety System were analyzed for adverse events occurring during olanzapine treatment through May 31, 2007. Proportional reporting ratios (PRR) and Chi-squares were calculated comparing adverse event frequencies in adolescents (13–17 years) and adults (18–64 years). Three criteria (≥1.0% frequency among all adolescent event reports, PRR≥2, and Chi-square ≥4) identified spontaneous adverse event report differences between adolescents and adults.
Results: Of total olanzapine spontaneous adverse events, 2.6% were reported in adolescents and 60.3% in adults. Remaining events included 9.0% in patients ≥65 years, 1.9% in patients <=12 years, and 26.2% where age was not reported. The most frequent reasons for olanzapine use in adolescents were schizophrenia, psychotic disorder and bipolar I disorder. Four events met criteria for potential differences in event reporting for adolescents: somnolence, aggression, galactorrhoea and sedation.
Conclusions: Somnolence, aggression, galactorrhoea, and sedation were the event terms meeting criteria for a potential difference in reporting in adolescent versus adult patients. Since product launch cumulatively through May 31, 2007, somnolence was rarely reported (frequency ≥0.01% and <0.1%). aggression, galactorrhoea, and sedation were very rarely reported (frequency <0.01%) in adolescents. Caution is warranted interpreting spontaneous event data because patient medical information may be incomplete and reporting bias or underreporting may occur.

doi:10.1016/j.schres.2007.12.388

322 – EFFICACY/TOLERABILITY OF PALIPERIDONE PALMITATE: 9-WEEK, PLACEBO-CONTROLLED STUDY IN SCHIZOPHRENIA PATIENTS

M. Kramer[1], R. Litman[2], R. Lane[3], **M. Kujawa**[1], P. Lim[1], D. Hough[1], M. Eerdekens[4].

[1]*Johnson & Johnson Pharmaceutical Research and Development, Titusville, NJ, USA*
[2]*CBH Health, LLC, Rockville, Maryland, USA*
[3]*Johnson & Johnson Pharmaceutical Research and Development, Raritan, NJ, USA*
[4]*Johnson & Johnson Pharmaceutical Research and Development, Beerse, Belgium*

Presenting Author details: mkujawamd@aol.com
1125 Trenton-Harbourton Road, 08560 Titusville, United States,
Tel.: +1 609 730 2442.

Background: This study evaluated the efficacy and safety of paliperidone palmitate, a long-acting injectable agent, in the treatment of patients with schizophrenia.
Methods: A 9-week, double-blind, placebo-controlled study, randomized schizophrenia patients ($N=197$ [intent-to-treat population], male=62%, mean±SD age=39.3±10.3 years) to receive 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 (baseline = 87.0 ± 12.5) and adverse event (AE) reporting, respectively.
Results: Mean ± SD PANSS total scores significantly improved ($p \leq 0.001$) from baseline 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 score at end point) were significantly greater in both paliperidone palmitate groups versus placebo ($p \leq 0.007$). AEs occurring ≥ 3% more with paliperidone palmitate than placebo (safety population, $N = 247$) were insomnia, schizophrenia, restlessness, sedation, extrapyramidal disorder, hypertonia, attention disturbance, electrocardiogram abnormal, constipation, myalgia, asthenia and vertigo. EPS-AE rates were comparable for paliperidone palmitate and placebo, with the exception of parkinsonism (7% and 1%, respectively). Serious AEs in ≥ 1 patient in any group were schizophrenia and psychotic disorder. Other serious AEs included elevated hepatic enzymes (placebo, $n = 1$), depression (50 mg eq., $n = 1$), suicidal ideation (50 mg eq., $n = 1$), psychomotor agitation (100 mg eq., $n = 1$) and syncope (100 mg eq., $n = 1$). No deaths occurred during the study.
Conclusions: Paliperidone palmitate (50 and 100 mg eq. doses) was effective and well tolerated in acute symptomatic schizophrenia.
Acknowledgement: Data previously presented at the U.S. Psychiatric & Mental Health Congress, 2007. Supported by funding from Johnson & Johnson Pharmaceutical Services, LLC, and Johnson & Johnson Pharmaceutical Research & Development.

doi:10.1016/j.schres.2007.12.389

323 – TAMOXIFEN — A POTENTIAL TREATMENT FOR WOMEN IN THE MANIC PHASE OF BIPOLAR AFFECTIVE DISORDER?

J. Kulkarni[1], L. Mu[1], A. De Castella[1], C. Gurvich[1], P. Fitzgerald[1], S. Davis[2].

[1]*Alfred Psychiatry Research Centre, The Alfred Hospital and the School of Psychology, Psychiatry and Psychological Medicine, Monash University, Melbourne Australia*
[2]*Department of Medicine, Alfred Hospital and Department of Obstetrics and Gynaecology, Faculty of Medicine, Nursing and Health Sciences, Monash University, Melbourne Australia*

Presenting Author details: j.kulkarni@alfred.org.au
The Alfred Hospital, Level One, Old Baker Building, Commercial Road, 3004 Melbourne, Australia,
Tel.: +61 3 9076 6924; fax: +61 3 9076 6588.

Background: Bipolar Affective Disorder (BPAD) is an illness with high morbidity and mortality. Lithium and other mood stabilizers are the main treatments for BPAD, despite little being known about their mechanisms of action. Recent attempts to elucidate the biochemical actions of these drugs have focused on the Protein Kinase C (PKC) pathways. Another PKC inhibitor hypothesized to be effective in the treatment of mania is tamoxifen, a selective estrogen receptor modulator with estrogen receptor antagonist actions in the CNS. The aim of the current study was to compare the effectiveness of two adjunctive antiestrogen agents (tamoxifen and progesterone) to placebo in the treatment of acute mania.
Methods: Women in the manic phase of BPAD or schizoaffective disorder were included in this 28-day, three-arm (40 mg/day oral tamoxifen or 20 mg/day oral progesterone or oral placebo) double-blind, placebo controlled and adjunctive study. All patients also received a mood stabilizer as the baseline treatment. Manic, psychotic and depressive symptoms were measured weekly using the Clinician Administered Rating Scale for Mania (CARS-M), Positive and Negative Syndrome Scale (PANSS) and Montgomery–Asberg Depression Rating Scale (MADRS) rating scales respectively, as were estrogen, progesterone and gonadotrophin levels. Cognitive functioning (RBANS) was assessed in a sub-sample of participants at baseline and repeated on day 28.
Results: Results of 43 women indicated a decline in the symptoms of mania and psychopathology in the tamoxifen group and to a lesser extent in the progesterone and control groups.
Conclusions: The results suggest that tamoxifen may be a useful adjunct in the treatment of acute manic symptoms in women with BPAD.
Acknowledgements: This research is supported by The Stanley Medical Research Institute.

doi:10.1016/j.schres.2007.12.390

324 – ADEPT: A DEFINITIVE ESTROGEN PATCH TRIAL

J. Kulkarni[1], C. Gurvich[1], F. Mehmedbegovic[1], A. De Castella[1], P. Ftizgerald[1], H. Burger[2].

[1]*The Alfred Psychiatry Research Centre, The Alfred and Monash University School of Psychology, Psychiatry and Psychological Medicine, Melbourne, Australia*
[2]*Prince Henry's Institute, Monash Medical Centre, Melbourne, Australia*

Presenting Author details: j.kulkarni@alfred.org.au
The Alfred Hospital, Level One, Old Baker Building, Commercial Road, 3004 Melbourne, Australia,
Tel.: +61 3 9076 6924; fax: +61 3 9076 6588.

Introduction: Accumulating evidence suggests estrogens may have therapeutic effects in severe mental illnesses, including schizophrenia, via neuromodulatory and neuroprotective activity. We will present the results of two research trials comparing the effectiveness of adjunctive transdermal estradiol (100 or 200 μg/day) to adjunctive placebo, in the treatment of acute psychotic symptoms.
Methods: For the first study, women of childbearing age with a diagnosis of schizophrenia or schizoaffective disorder were invited to participate in a 4-week, double-blind, placebo controlled study. Women were randomized to receive either 100 mcg transdermal adjunctive estradiol (56 women), or adjunctive transdermal placebo (46 women), for a 28-day trial period (and all patients continued to receive their standard antipsychotic treatment). Assessments were conducted at baseline, then at days 7, 14, 21 and 28, and included psychopathology (PANSS) and mood (MADRS) ratings, as well as measures of estrogen, progesterone, and gonadotropin levels. A cognitive battery was also completed at each assessment. The subsequent trial is ongoing and involves a similar patient population, participating in an 8-week, three-arm (100 μg/day adjunctive transdermal estradiol, 200 μg/day adjunctive transdermal estradiol, or adjunctive transdermal placebo) double-blind, placebo controlled study. The previously described assessment battery is conducted at baseline, then at days 7, 14, 28 and 56.