**PM418**

**Efficacy of Lurasidone in Patients With Schizophrenia With Prominent Positive Symptoms: A Pooled Analysis of Short-Term Placebo-Controlled Studies**

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**Topic:** Clinical

**Sub-Topic by Disorder:** Schizophrenia

**Sub-Topic by Drug and Methodology:** Antipsychotics

**Abstract**

**Objective:** This post hoc analysis evaluated the efficacy of lurasidone in patients with acute schizophrenia with prominent positive symptoms.

**Methods:** Patient-level data were pooled from 5 similarly designed, multinational, randomized, double-blind, placebo-controlled, 6-week studies of fixed-dose lurasidone (40, 80, 120, or 160 mg/d) in adult patients with acute schizophrenia. Patients with prominent positive symptoms were defined as those with baseline Positive and Negative Syndrome Scale (PANSS) positive subscale score > negative subscale score. Treatment response was defined as ≥30% decrease from baseline in PANSS total score at week 6 (last observation carried forward [LOCF]).

**Results:** This analysis included 919 patients with and 613 patients without prominent positive symptoms. Based on change from baseline to week 6 in PANSS total score (mixed-model repeated-measures analysis), effect sizes for lurasidone 40, 80, 120, and 160 mg/d were 0.51, 0.65, 0.44, and 1.09, respectively, for patients with prominent positive symptoms (all P<0.001) and 0.29, 0.46, 0.55, and 0.67, respectively, for patients without prominent positive symptoms (P<0.05 for 40 mg/d; all other P<0.001). In patients with prominent positive symptoms, treatment response at week 6 LOCF was observed in 29.3% of patients in the placebo group and 48.3%, 46.6%, 43.2%, and 64.4% of patients in the lurasidone 40, 80, 120, and 160 mg/d groups, respectively (with associated number needed to treat [NNT] of 6, 6, 8, and 3, respectively). In patients without prominent positive symptoms, treatment response at week 6 LOCF was observed in 35.7% of patients in the placebo group and 50.0%, 52.1%, 54.5%, and 60.4% of patients in the lurasidone 40, 80, 120, and 160 mg/d groups, respectively (NNT of 7, 7, 6, and 5, respectively).

**Conclusions:** In this analysis of patients with schizophrenia, lurasidone therapy was associated with larger effect sizes in patients with versus without prominent positive symptoms.

**Support:** Sunovion Pharmaceuticals Inc.

**Disclosures**

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**PM419**

**Efficacy and safety of paliperidone palmitate 3-monthly versus 1-monthly formulation in Asian patients with schizophrenia: Subgroup analysis of a randomized, double-blind, noninferiority study**

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**Abstract**

**Background:** The current study was designed to demonstrate noninferiority of paliperidone palmitate 3-monthly formulation (PP3M) to PP 1-monthly formulation (PP1M) in Asian patients (China, Japan, Korea and Taiwan) with schizophrenia.

**Methods:** Eligible patients (18–70 years) entered 17-week, flexible-dose, open-label (OL) phase to receive PP1M. Stabilized patients were randomized (1:1) to receive fixed doses of PP1M or PP3M (175, 263, 350, or 525 mg eq.) in a 48-week, double-blind (DB) phase.

**Results:** Total 510 Asian patients were enrolled and dosed in OL phase (total population: n=1429; China: n=296, Japan: n=175, Korea: n=19, Taiwan: n=20); 344 Asian patients were randomized in DB phase (total population: PP3M=504, PP1M=512, China: PP3M=104, PP1M=106, Japan: PP3M=52, PP1M=56, Korea: PP3M=7, PP1M=5, Taiwan: PP3M=7, PP1M=7). The Kaplan-Meier estimate of the difference (95% CI) between the treatment groups (PP3M-PP1M) in percentages of patients who remained relapse free (primary efficacy endpoint) was similar in the larger 2 subgroups (China: 1.1% [-6.1%; 8.3%]; Japan: 5.1% [-12.0%; 22.2%]) and the total population (-11.2% [-27.1%; 5.1%]). The lower bounds of the 95% CI for all subgroups were larger than the pre-specified non-inferiority margin of -15%. Incidences of treatment-emergent adverse events (TEAEs) during the OL phase (China: 198/296 [66.9%]; Japan: 132/175 [75.4%]; as well as DB phase (China: 149/210 [71.0%]; Japan: 99/108 [91.7%]) were higher in the larger 2 subgroups versus the total population (OL total population: 846/1429 [59.2%]; DB total population: 682/1016 [67.1%]). Increased weight was the most frequent (≥20%) TEAE during the DB phase (PP3M vs. PP1M, China: 36.5% vs. 34.9%; Japan: 25.0% vs. 19.6%).

**Conclusions:** PP3M was non-inferior to PP1M and was similarly tolerable in both total population, and Asian patients with schizophrenia.

**PM420**

**Additional clinical effects of long-term clozapine therapy for chronic schizophrenia**

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**Abstract**

**Objectives:** The aim of this study was to investigate any possible additional effects of long-term use of clozapine and to figure out the factors related to additional improvement after 6 months.

**Methods:** 31 inpatients with schizophrenia who have taken clozapine over 1 year were recruited, and changes of their symptom severity were assessed with Brief Psychiatric Rating Scale (BPRS).

**Results:** The current study was designed to demonstrate noninferiority of paliperidone palmitate 3-monthly formulation (PP3M) to PP 1-monthly formulation (PP1M) in Asian patients (China, Japan, Korea and Taiwan) with schizophrenia.

**Results:** Total 510 Asian patients were enrolled and dosed in OL phase (total population: n=1429; China: n=296, Japan: n=175, Korea: n=19, Taiwan: n=20); 344 Asian patients were randomized in DB phase (total population: PP3M=504, PP1M=512, China: PP3M=104, PP1M=106, Japan: PP3M=52, PP1M=56, Korea: PP3M=7, PP1M=5, Taiwan: PP3M=7, PP1M=7). The Kaplan-Meier estimate of the difference (95% CI) between the treatment groups (PP3M-PP1M) in percentages of patients who remained relapse free (primary efficacy endpoint) was similar in the larger 2 subgroups (China: 1.1% [-6.1%; 8.3%]; Japan: 5.1% [-12.0%; 22.2%]) and the total population (-11.2% [-27.1%; 5.1%]). The lower bounds of the 95% CI for all subgroups were larger than the pre-specified non-inferiority margin of -15%. Incidences of treatment-emergent adverse events (TEAEs) during the OL phase (China: 198/296 [66.9%]; Japan: 132/175 [75.4%]; as well as DB phase (China: 149/210 [71.0%]; Japan: 99/108 [91.7%]) were higher in the larger 2 subgroups versus the total population (OL total population: 846/1429 [59.2%]; DB total population: 682/1016 [67.1%]). Increased weight was the most frequent (≥20%) TEAE during the DB phase (PP3M vs. PP1M, China: 36.5% vs. 34.9%; Japan: 25.0% vs. 19.6%).

**Conclusions:** PP3M was non-inferior to PP1M and was similarly tolerable in both total population, and Asian patients with schizophrenia.

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**Additional clinical effects of long-term clozapine therapy for chronic schizophrenia**

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**Abstract**

**Objectives:** The aim of this study was to investigate any possible additional effects of long-term use of clozapine and to figure out the factors related to additional improvement after 6 months.

**Methods:** 31 inpatients with schizophrenia who have taken clozapine over 1 year were recruited, and changes of their symptom severity were assessed with Brief Psychiatric Rating Scale (BPRS).
Efficacy and safety of brexpiprazole (OPC-34712) in acute schizophrenia: a pooled analysis of two pivotal studies

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Abstract

Background: Brexpiprazole is a serotonin-dopamine activity modulator that acts as a partial agonist at 5-HT1A and dopamine D2 receptors, and an antagonist at 5-HT2A and noradrenaline alpha1B/2C receptors, all at similar potencies. The efficacy, safety, and tolerability of brexpiprazole were evaluated in patients with acute schizophrenia, based on pooled data from two pivotal phase III studies (NCT01396421[1] and NCT01393613[2]).

Methods: In two similarly designed studies, patients with acute schizophrenia were randomly assigned to fixed once-daily doses of brexpiprazole 2mg, 4mg or placebo (an additional treatment group was included in each study [0.25mg and 1.0mg] to evaluate the dose range; these doses were not included in the meta-analysis). Primary efficacy endpoint was change in PANSS total score from baseline to week 6; key secondary endpoint was the change in CGI-S score at week 6.

Results: Pooled brexpiprazole 4mg (N=359) and 2mg (N=359) were each superior to placebo (N=358) in change from baseline in PANSS total score at week 6 (least square mean difference [LSMD] to placebo: -6.69, p<0.0001 and -5.46, p=0.0004, respectively). Results of the key secondary endpoint supported the primary results.

Conclusion: From the results above, some patients with schizophrenia benefit from maintaining clozapine over 6 months. Though no factors predictive of additional efficacy were found, this work suggests it is worth maintaining clozapine over 6 months for some patients if there are no other probable options left in clinical setting.

References
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2. Kane et al., Schizophrenia Res 2015;164:127–135

Corticostereoids in treatment of schizophrenia – who is benefited from blonanserin augmentation?: An open-label, prospective, multicenter study

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Abstract

Several previous case reports have shown that clozapine treatment occasionally induces elevation of creatine phosphokinase (CPK) levels. We describe a patient with marked elevations of CPK following initiation of clozapine treatment.

The case was a 41-year-old woman who was first diagnosed with schizophrenia at the age of 25 due to auditory hallucination and delusions of persecution. She was admitted to our psychiatric ward at the age of 41 due to aggressive behaviors and worsening of psychotic symptoms. Treatment with antipsychotics including quetiapine, olanzapine, and aripiprazole as well as electroconvulsive therapy was ineffective in relieving her symptoms. Clozapine was begun on day 162 of admission at the dose of 12.5mg/day and was gradually increased to 600mg/day by day 232. On day 286, she had a generalized tonic-clonic seizure. Because she had no past history of epilepsy, we suspected clozapine to be the cause of the seizure. Therefore, the dose was decreased to 400mg/day the following day. Her serum levels of CPK were 1079 U/L, 6454 IU/L, and 7509 U/L on days 287, 290, and 291, respectively. Clozapine was discontinued on day 291. Serum CPK level decreased to 5224 U/L on day 293. An isoenzyme study showed that the CPK was almost exclusively of skeletal muscle origin. Malignant syndrome was unlikely due to the lack of fever, rigidity, and increased white blood cell count. Because clozapine was the only effective treatment for her psychotic symptoms, clozapine was restarted on day 297. After 56 days of treatment with clozapine 400mg/day, no relapse of seizures or CPK elevation has been observed.

An elevated CPK level is one of the adverse events observed in those prescribed clozapine. However, readministration of clozapine with close monitoring after the occurrence of such adverse effect may be a treatment option.

Blinonserin augmentation in patients with schizophrenia – who is benefited from blonanserin augmentation?: An open-label, prospective, multicenter study

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