Efficacy 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 change in CGI-S score at 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.

Altogether 8.2% (30/364) and 7.1% (26/368) of brexpiprazole-treated patients (4mg and 2mg, respectively) vs 14.7% (54/368) of placebo-treated patients discontinued due to adverse events. The incidences of insomnia and agitation in the brexpiprazole treatment groups were similar or lower than with placebo. Akathisia incidences were 6.9% and 4.6% in the brexpiprazole 4mg and 2mg groups, respectively, vs 4.6% with placebo and sedation incidences were 2.7% and 1.6% in the brexpiprazole 4mg and 2mg groups, respectively, vs 0.8% with placebo.

Conclusion: Pooled data from two pivotal studies provide evidence that brexpiprazole is efficacious and safe in treating patients with acute schizophrenia. Both brexpiprazole 2 and 4mg were well tolerated, with notably low levels of akathisia and sedation.

References
1. Correll et al., Am J Psychiatry 2015;172:870–880
2. Kane et al., Schizophrenia Res 2015;164:127–135

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Creatine Phospho Kinase Elevations with Clozapine

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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 electroconvulsivetherapy 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 lU/L, and 7509U/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.

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

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