165th American Psychiatric Association (APA) Annual Meeting

Once-Monthly Depot Atypical Antipsychotic Is Expected to Expand Options for Chronic Control of Schizophrenia

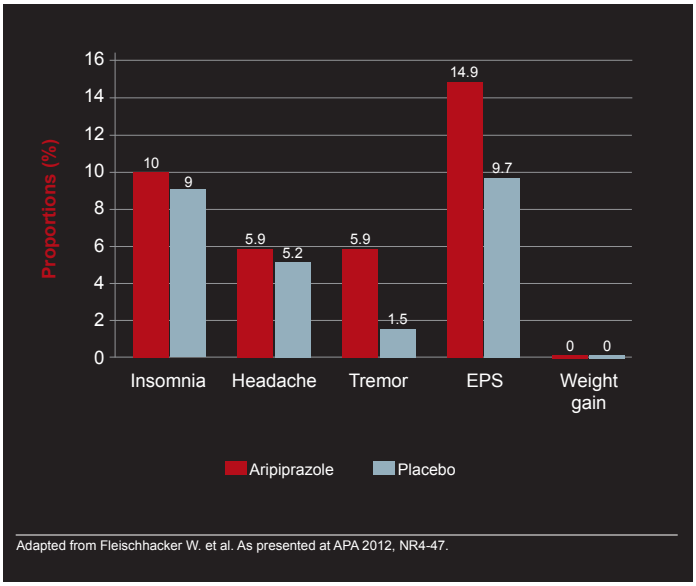
Philadelphia - A phase III study associated a once-monthly injection of an atypical antipsychotic with protection against relapse of schizophrenia with a remarkably benign safety profile. The study was conducted on an atypical antipsychotic that has demonstrated a low risk of weight gain and metabolic disturbances relative to other atypical agents. While the first once-monthly injectable antipsychotic paliperidone, which is an active metabolite of risperidone, was approved almost three years ago, the expanding number of options for a depot approach to long-term disease control could reduce the relapses due to non-adherence.

"The specific results of this study were encouraging because of the highly-significant protection against relapse combined with a side effect profile that was comparable to placebo," reported Dr. John Kane, Vice President, Behavioral Health Services, North Shore-LIJ Health System, New Hyde Park, NY. Senior author of the study, Dr. Kane explained that the 52-week study was conducted in phases in which all patients were stabilized on oral aripiprazole before being randomized in a 2:1 ratio to every-four-week intramuscular (IM) depot injections of aripiprazole or placebo. Of the 710 patients initially recruited for the trial, 403 were randomized and followed long-term.

The rate of impending relapse, which was the primary endpoint, was 10% in the aripiprazole group and 39.6% ($P<0.0001$) over the course of the one-year study. The improvements in Positive and Negative Syndrome Scale (PANSS) that were achieved in the stabilization phase fell on average by only 1.6 points in the aripiprazole group versus 11.6 points ($P<0.0001$) in the placebo group. Other significant differences in secondary outcomes favouring the agent, such as measures of social functioning ($P=0.0002$), reinforced the persistence of the long-term efficacy of the once-monthly injections.

Relevant to aripiprazole, a dopamine partial agonist with a broad spectrum of activity reflected in indications for bipolar disease, major depression, and irritability associated with autism in children in addition to schizophrenia, the relatively favourable safety and tolerability profile was preserved in the IM monthly injections. In a separate safety analysis presented by Dr. Wolfgang Fleischhacker, Director, Department of Psychiatry, Medical University of Innsbruck, Austria, the most common side effects, such as insomnia (10% vs. 9%) and headache (5.9% vs. 5.2%), occurred in similar rates in the aripiprazole and placebo groups. Tremor (5.9% vs. 1.5%) and EPS (14.9% vs. 9.7%) were more common on aripiprazole but differed modestly. There was a slight weight loss in both groups (Figure 1).

FIGURE 1 I IM Aripiprazole Tolerability Differs Modestly from Placebo



Adapted from Fleischhacker W. et al. As presented at APA 2012, NR4-47.

"There were no unusual shifts in laboratory values or fasting metabolic parameters across any study phase," Dr. Fleischhacker reported. "These data suggest that the IM aripiprazole formulation offers a new option with a different risk-benefit profile than currently available treatments."

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