SAN DIEGO -- Bifeprunox, an investigational atypical antipsychotic agent, was significantly better than placebo at preventing deterioration of schizophrenia over six months and had a good metabolic profile.

And unlike other atypical agents, bifeprunox does not appear to be associated with adverse metabolic effects: Patients on the drug lost weight and had decreases in body mass index over the course of the study, reported Daniel Casey, M.D., from Oregon Health & Science University, in Portland, at the American Psychiatric Association meeting here.

The drug was also associated with a favorable lipid profile, including no increase in LDL, and a small rise in HDL, Dr. Casey and colleagues said.

"The increases in the good cholesterol were modest, but in the right direction, whereas we've seen decreases in good cholesterol with some other atypical antipsychotics. Those decreases were modest, but qualitatively, they're going in the wrong direction," said Dr. Casey.

Bifeprunox, like aripiprazole (Abilify), is a dopamine partial agonist, with a similar mechanism of action, Dr. Casey said.

He and his colleagues compared bifeprunox, in 20 and 30 mg doses given once daily, with placebo over six months in 497 stable patients with schizophrenia.

Patients were considered to be stable if they had had a diagnosis of schizophrenia for at least two years, no change in antipsychotic agents or dose for at least 30 days before screening, no modification of treatment management or significant improvement or worsening over the last three months, a Positive and Negative Syndrome Scale score of 60 or higher and scores of 4 or lower on that scale's hostility and uncooperativeness items, and had a score of 4 or greater on the Clinical Global Impression-Severity of Illness scale.

In the double blind, parallel group study, the investigators randomly assigned patients to receive bifeprunox in one of the two doses, or placebo.

The primary efficacy endpoint measure was time to deterioration from randomization, with deterioration defined as fulfillment of one or more of the following: a Clinical Global Impression-Improvement score of 5 or greater, a Positive and Negative Syndrome Scale item P7 (hostility) and/or G8 (uncooperativeness) score of 5 or greater for two consecutive days, or at least a 20% increase in the scale score from baseline.

The authors also looked at the change in Positive and Negative Syndrome Scale total score at week six, and evaluated the drug for adverse events, extrapyramidal symptoms, weight and BMI, laboratory results, and vital signs.

They found that treatment with bifeprunox at both dose levels resulted in a statistically significantly longer time to deterioration of schizophrenia than placebo (20 mg dose, P=0.008, 30 mg dose, P=0.006).
Deterioration rates at six months were 41% for bifeprunox 20 mg, 38% for 30 mg, and 59% for placebo. In addition, bifeprunox showed a statistically significant difference from placebo in Positive and Negative Syndrome Scale total score by week 6, and at every subsequent time point during the six-month study.

"There were statistically significant differences between bifeprunox and placebo in positive and negative Positive and Negative Syndrome Scale subscales and the Brief Psychiatric Rating Scale scores at endpoint.

In all, 72.3% of patients on bifeprunox 20 mg and 83.1% of those on the 30 mg dose had at least one treatment-emergent adverse event, compared with 57.8% of patients on placebo.

The most common adverse events with bifeprunox, occurring in at least 5% of patients and with at least twice the frequency of patients on placebo, included nausea, vomiting, dizziness, anorexia, akathisia, dyskinesia and asthenia. Prolactin levels decreased in all treatment groups.

Bifeprunox 30 mg significantly improved fasting triglyceride levels from baseline compared to placebo, with a mean change of -35.4 for bifeprunox, vs. - 4.4 for placebo (P=0.006). In addition, patients on bifeprunox 30 mg had significant decreases in both weight and BMI compared with placebo (P

"Results from this study suggest that bifeprunox may be an efficacious, safe, and well-tolerated long-term treatment option for stable patients with schizophrenia," the authors concluded.

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