新たな統合失調症治療薬

Phase 3トライアルの結果、lurasidoneは統合失調症治療において有効であり忍容性も良好であることが示された

Phase 3 trial finds lurasidone to be effective and well tolerated for treatment of schizophrenia

急性期の統合失調症治療に対するlurasidoneの初めてのphase 3トライアルの結果、この薬剤がプラセボよりも有意に有効であり忍容性も良好で脱落率も比較的低いことが報告された、と第162回American Psychiatric Association学会で発表された。無作為化プラセボコントロール二重盲検多国籍トライアルPEARL 1 ：Program to Evaluate the Antipsychotic Response to Lurasidone（Lurasidoneの抗精神病作用を評価するプログラム）において急性期の統合失調症患者に一日40mg、80mg、120mgのいずれかの用量のlurasidoneを6週間投与しプラセボと比較し評価した。一日80mgのlurasidone投与により、Positive and Negative Syndrome Scale（PANSS）総スコア（一次エンドポイント）およびClinical Global Impressions Severity scale（CGI-S、重要な二次エンドポイント）が第2週から第6週までの全ての受診時において改善していた。lurasidoneの体重への影響はプラセボと同等であり（体重変化中央値はlurasidone群全体で0.3kgに対しプラセボ群で0kg）、脂質および血糖値に対する影響も同等であった。またlurasidone群全体の脱落率はプラセボと比較し低く（31%対43%）忍容性が良好であり、有害事象による脱落率も低かった（lurasidone群全体とプラセボ群とでそれぞれ6%と2%）。

Full Text

The first phase 3 trial of lurasidone for treatment of acute schizophrenia reports the drug is significantly better than placebo, was well tolerated and has a relatively low discontinuation rate according to findings presented at the 162nd Annual Meeting of the American Psychiatric Association.

PEARL 1 (Program to Evaluate the Antipsychotic Response to Lurasidone) is part of an extensive worldwide phase 3 clinical development program, involving more than 2,000 patients, intended to evaluate the safety and efficacy of lurasidone for the treatment of schizophrenia. In addition to the primary finding of this six-week, double-blind, placebo-controlled trial that lurasidone 80 mg/day was significantly more effective than placebo at the study endpoint, lurasidone was associated with greater improvement on both the Positive and Negative Syndrome Scale (PANSS) total score (primary endpoint) and the Clinical Global Impressions Severity scale (CGI-S, key secondary endpoint) at all visits between weeks two and six. PEARL 1 also evaluated two other fixed doses of lurasidone, 40 mg/day and 120 mg/day, which did not demonstrate separation from placebo on the PANSS or CGI-S at study endpoint.

"People with schizophrenia need new treatment options that offer a combination of efficacy, safety and tolerability so that the symptoms can be stabilized and effectively treated," said Henry Nasrallah, M.D., professor of psychiatry and neuroscience and director of the schizophrenia research program at the University of Cincinnati College of Medicine. "Lurasidone has the potential to be an important new therapeutic option for patients with schizophrenia."

Lurasidone's effect on weight was similar to placebo (median change 0.3 kg for overall lurasidone group vs. 0 kg for placebo) as was its effect on lipid and glucose measures. Lurasidone was also well tolerated with a lower overall discontinuation rate (31%) compared to placebo (43%) and few adverse event-related discontinuations (6% and 2% for the overall lurasidone group and placebo, respectively).

Adverse events seen in the trial were generally mild. The most commonly reported adverse events for lurasidone (greater than 5% and at least twice the rate of placebo) were akathisia (17.6% vs. 3.1% placebo), somnolence (11.7% vs. 5.5%), parkinsonism (6.8% vs. 0), and increased weight (5.1% vs. 2.4%).

"The development program for lurasidone is intended to establish efficacy for the core symptoms of schizophrenia, characterize its safety profile and explore its effects in the treatment of cognitive impairment and other areas not adequately addressed by current therapies," said Antony Loebel, M.D., vice president of clinical research, Dainippon Sumitomo Pharma America, Inc. "As a large, global trial, the PEARL 1 study is an important new addition to the existing clinical trial database."

This randomized, placebo-controlled, double-blind, multinational clinical trial evaluated the efficacy and safety of lurasidone 40 mg, 80 mg and 120 mg once daily compared to placebo, over six weeks in patients with acute schizophrenia. Patients were diagnosed with schizophrenia (using DSM-IV criteria) and were required to have an acute exacerbation of psychotic symptoms with a PANSS total score of 80 or higher at study baseline.

A total of 500 patients were randomized equally to the four treatment arms. The pre-specified primary endpoint was change from baseline in the PANSS total score over the six-week study duration for each lurasidone dose group vs. placebo. A key secondary endpoint was the change from baseline in CGI-S over the six-week study period. Efficacy data were statistically analyzed using a mixed model for repeated measures. Multiple safety assessments were done, including vital signs, weight, ECGs, movement disorder scales (SAS, BAS, AIMS), and laboratory assessments.

The study was conducted at 51 sites worldwide. Twenty-two sites in the United States randomized 278 patients, 21 sites in Europe randomized 148 patients and eight sites in Asia randomized 48 patients. The majority of trial participants were male with a mean age of 39 years. The mean time since initial diagnosis was approximately 14 years, and patients had, on average, four or more hospitalizations prior to study entry.

Lurasidone has been studied in three double-blind, placebo-controlled, six-week trials involving more than 650 patients with schizophrenia, of which 392 patients received lurasidone. Two of the three studies demonstrated that lurasidone had superior efficacy compared to placebo at doses ranging between 40 mg and 120 mg/day. A third study, which examined three fixed doses of lurasidone (20 mg, 40 mg, and 80 mg/day) did not show statistical differences vs. placebo. This trial is regarded as "failed," or inconclusive, as haloperidol (10 mg/day), which was included for purposes of assay sensitivity, also failed to distinguish from placebo.