SYNOPSIS

Synoptic Clinical Study Report Phase E CN138032

TITLE OF STUDY: A Multicenter, Randomized, Double-Blind Study of Flexible Doses of Aripiprazole Versus Perphenazine in the Treatment of Patients with Treatment-Resistant Schizophrenia (Phase E of Protocol CN138032)

INVESTIGATORS AND STUDY CENTERS: Forty-seven investigators in the United States of America and Canada enrolled patients in the study.

PUBLICATIONS: None

STUDY PERIOD: Date first patient enrolled Phase E: 28-Nov-2000
               Date last patient completed Phase E: 28-May-2003

CLINICAL PHASE: 3

OBJECTIVES: The primary objective of the study was to assess the long-term safety of aripiprazole in treatment-resistant schizophrenia patients who completed Phase D. The secondary objective was to assess the long-term efficacy of aripiprazole in treatment-resistant schizophrenia patients who completed Phase D.

• METHODOLOGY: There were 5 phases to Study CN138032:
  • Phase A: Patients participated in a 2-14 day screening period with minimum 2-day neuroleptic washout
  • Phase B: Patients were assigned open-label olanzapine or risperidone for 6 weeks/42 days
  • Phase C: Patients not responding to open-label treatment with olanzapine or risperidone in Phase B received single-blind placebo for minimum 2 days
  • Phase D: Patients were assigned to double-blind aripiprazole (15 or 30 mg/day) or perphenazine (8 - 64 mg/day) for 6 weeks
  • Phase E: Patients who completed Phase D were eligible to receive open-label aripiprazole (15 or 30 mg/day) for an additional 109 weeks during Phase E

NUMBER OF PATIENTS TREATED: Two-hundred twelve patients entered Phase E, and 211 patients received aripiprazole.

RESULTS:

Efficacy: No efficacy analyses were performed during Phase E.

Safety: Patients were analyzed by prior treatment (perphenazine or aripiprazole). The most frequently occurring treatment-emergent adverse events (AEs) (≥ 10% incidence in any prior treatment group) in Phase E were:

• Prior Perphenazine: insomnia (28%), psychosis (22%), agitation (14%), headache (14%), anorexia (11%), anxiety (10%)
Prior Aripiprazole: insomnia (25%), agitation (17%), psychosis (16%), anxiety (11%), headache (11%), and akathisia (11%)

Three patients died during Phase E; none of the deaths was considered related to study medication: 1 patient from pancreatic cancer 10 days after the last dose of aripiprazole; 1 patient from cardiac arrest 7 days after the last dose of aripiprazole; and 1 patient from accidental injury (ingestion of neutral disinfectant solution) 27 days after the last dose of aripiprazole. One patient became pregnant during the study.

Of the 69 patients who experienced serious adverse events (SAEs), 8 had events that were considered related (possibly, probably, certainly) to study medication: 3 patients in the prior perphenazine group (weight loss, hallucination, and psychosis) and 5 patients in the prior aripiprazole group (3 psychosis, 1 seizure grand mal, and 1 creatine phosphokinase [CPK] increased).

The most common reasons for discontinuation were psychosis (15% prior perphenazine and 6% prior aripiprazole) and reaction schizophrenic (3% prior perphenazine and 4% prior aripiprazole). The investigators considered most events to be unrelated to study medication.

The incidence of potentially clinically relevant laboratory abnormalities was low, except for parameters of elevated CPK (8% overall: 12% prior perphenazine; 3% prior aripiprazole) and elevated prolactin (7% overall: 5% prior perphenazine; 8% prior aripiprazole). There were no clinically meaningful differences between the groups on vital sign or electrocardiogram measures.

CONCLUSIONS:

- Aripiprazole was safe for long-term use in treatment-resistant schizophrenia patients as demonstrated by the low incidence of SAEs and discontinuations due to AEs. No clinically meaningful differences were noted between patients who received treatment with prior perphenazine and prior aripiprazole.
- Clinical evaluation of laboratory tests, vital sign measurements, and ECG assessments (including QTc) revealed no safety concerns for aripiprazole.

DATE OF REPORT: 10-Mar-2006