

## CASE STUDY

### **A 6-Week, Multi-centre, Double-blind, Double-dummy, Active-Controlled Randomized Study to Evaluate the Efficacy and Safety of XXXX compared to YYYY in the Treatment of Patients with Acute Episode of Schizophrenia (Hospitalized)**

Phase III trial

10 sites (US, Canada, UK), 250 patients

1 yearr enrollment

#### **Objectives**

The primary objective of this study is to evaluate the efficacy of XXXX, administered once daily, compared to YYYY, administered twice daily in the treatment of patients with an acute episode of schizophrenia.

The primary outcome variable will be the change from baseline of the Positive and Negative Syndrome Scale (PANSS) total score at the end of treatment at Day 42.

The secondary objectives of the study are to evaluate the following:

#### **Efficacy:**

- The efficacy of XXXX compared to YYYY in reducing positive, negative and general psychopathological symptoms, and aggression, hostility, depression in the treatment of schizophrenic patient with acute episode
- The response rate of XXXX compared to YYYY in the treatment of patients with an acute episode of schizophrenia
- The efficacy of XXXX compared to YYYY in improving overall clinical status of schizophrenia in the treatment of patients with an acute episode of schizophrenia

#### **Safety**

The safety and tolerability of XXXX compared to YYYY in the treatment of patients with an acute episode of

#### **Target subject population**

Male or female patient, 18 to 65 years of age, inclusive, with a diagnosis of schizophrenia by the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) criteria (Schizophrenia [DSM-IV]: disorganized [295.10]; catatonic [295.20]; paranoid [295.30]; undifferentiated [295.90]) will be enrolled. The patients should also have a PANSS total score of  $\geq 70$  and at least 4 on one or more of the following PANSS items: P1 - delusions; P2 - conceptual disorganization; P3 - hallucinatory behavior; P6 - suspiciousness/persecution at Visit 1 (screening) and 2 (randomization). Approximate 250 patients from 10 sites will be randomized (1:1) into one of the two treatment group.

### **Duration of treatment**

After the enrolment visit and screening period of up to 7 days, the patient will be randomized on Day 1 to one of two treatments groups. Dosing will consist of a 1-week titration period followed by a 5-week flexible dose period. The total randomized treatment duration is 42 days.

### **Primary outcome variable**

The primary outcome variable will be the change from baseline in Positive and Negative Syndrome Scale (PANSS) total score at the end of treatment at Day 42. (LOCF)

### **Secondary outcome variables:**

- Change from baseline in PANSS positive, negative, general psychopathological subscale score at the end of treatment at Day 42. (LOCF)
- Change from baseline in PANSS aggression, hostility and depression clusters score at the end of treatment at Day 42. (LOCF)
- Proportion of patients achieving a reduction of at least 30% from baseline PANSS total score at the end of treatment at Day 42. (LOCF)
- Change in the CGI Severity of Illness score from baseline at the end of treatment at Day 42. (LOCF)
- Proportion of patients with CGI Global Improvement rating  $\leq 3$  at the end of treatment at Day 42. (LOCF)

### **Safety outcome variables**

- The incidence of adverse events (AEs)
- Clinically significant changes in hematology, clinical chemistry (including thyroid function test, glycosylated hemoglobin (HbA1c), fasting plasma glucose, fasting lipid levels and prolactin levels), vital signs (including blood pressure, pulse and weight) and electrocardiogram (ECG) results
- Extrapyramidal symptoms (EPS), adverse events related to EPS, changes in EPS related scales i.e., Simpson-Angus Scale (SAS) and Barnes Akathisia Rating Scale (BARS), and the proportion of patients using anticholinergic medication.

### **Statistical methods**

Statistical analysis on efficacy endpoints will be performed using Full Analysis Set (FAS) as the primary analysis and the per-protocol population (PP) for consistency check. Safety endpoints will be performed in the safety population. The FAS population will consist of all allocated to study treatment patients who receive at least one dose of study treatment and who have measurements at baseline and at least one post baseline PANSS assessment, PP population is defined as all FAS patients with no major protocol violations or deviations affecting efficacy. The safety population will consist of all patients allocated to study treatment who receive at least one dose of study treatment. Other secondary efficacy analyses as well as safety and tolerability analyses will be by means of descriptive statistics, frequency tables, and graphs as appropriate.

### **Visit Schedule**

A visit window of  $\pm 1$  days is allowed for the visit on Day 7, Day 14, Day 21, and Day 28 whereas  $\pm 2$  days allowed for the visit on Day 42. All visits are planned relative to Day 1, i.e., the days should be counted from the randomization date, not from last actual visit date. All visits should preferably be performed at the same time of the day for each patient throughout the study.

### **Restrictions**

Patients must remain inpatients for a minimum of 14 days immediately after randomization

### **Criteria for discontinuation**

Patients may be discontinued from study treatment and assessments at any time. Specific reasons for discontinuing a patient from this study are:

- Voluntary discontinuation by the patient who is at any time free to discontinue his/her participation in the study, without prejudice to further treatment
- Safety reasons as judged by the investigator and/or Sponsor
- Severe non-compliance to protocol as judged by the investigator and/or Sponsor
- Incorrect enrolment, i.e., the patient does not meet the required inclusion/exclusion criteria
- Any patient who, based on the Investigator's judgment, poses an imminent risk of suicide.
- Development of exclusion criteria, e.g. pregnancy.
- The patient is lost to follow-up i.e. the center is unable to reach the patient after three phone calls and one written letter sent by registered/certified mail, documented in the patient medical record.
- If a patient has a neutrophil count of  $<1.0 \times 10^9 /L$  after two repeated tests after 28 days of treatment. The second test should be performed within 24 hours after the laboratory results from the first test are received.
- The study is terminated by Sponsor, Regulatory Authorities or Independent Ethics Committees (IEC).