STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: Seroquel XR
ACTIVE INGREDIENT: Quetiapine fumarate

Study No: D1443L00060
Open-label multicentre study on efficacy and safety of oral quetiapine (Seroquel XR) in adults with schizophrenia

Developmental Phase: IIIb

Study Completion Date:
Date of Report: 08 February 2011

OBJECTIVES:

Primary objective was to evaluate the efficacy of Seroquel XR in the treatment of patients with schizophrenia. Secondary objective was to assess the safety and tolerability of Seroquel XR at the daily dose up to 600mg, oral administer, once a day, in the morning or evening time for 42 days.

METHODS:

This is a 6 week, multi-centre, open label, non-controlled study in the schizophrenic patients. The primary study endpoint is the change from baseline (Day 1) to the final assessment (Day 42 or withdrawal) in the Positive Negative Syndrome Scale (PANSS) total score. Efficacy, safety, tolerability were assessed. To be eligible for the study, a patient has to be diagnosed with acute schizophrenia as defined by Diagnostic and Statistical Manual of Mental Disorders, 4th edition, revised 1994 (DSM-IV), male or female patients, aged 18-65, and have a PANSS total score of at least 70 at screening and on Day 1. Patients also have to have a score of at least 4 at baseline on the Clinical Global Impression- Severity of Illness (CGI-S) item, with evidence of worsening in the 3 weeks before enrolment, indicating acute exacerbation.

Patients provided informed consent and were screened for eligibility (at Visit 1) up to7 days before baseline assessment on Day 1. On Day 1, baseline assessments were performed, and patients were assigned to Seroquel XR at 300mg. On Day 2, all patients were assigned to reach target dose of Seroquel XR at 600mg daily until Day 42. Each visit had ±3 days window period. Oral antipsychotic treatments have to be

discontinued at lease 1 dosing interval before baseline assessments. Patients treated wit Seroquel XR took the tablet once daily after evening meal. The primary efficacy assessment was based on PANSS total score on Day 1 (baseline) before the first dose of study medication is given and on Day 14 (Week 2), and Day 42 (Week 6). Secondary efficacy assessment are based on PANSS total and subscale score as well as on Clinical Global Impression (CGI), which were assessed along with PANSS score on screening, Day 1, 14, and 42. Safety was assessed throughout the study in terms of adverse events, laboratory assessments, and neurological findings.

Initially the study planned to enroll 100 patients. Because of administrative reasons, the study was terminated after 28 patients were enrolled. Due to small number of patients, all analyses are merely descriptive using frequency as well as summary measures such as mean and standard deviation for continuous variables and percent description for categorical variables.

RESULTS:

Among a total of 28 patients, 71.4% were male (20 males and 8 females). Their age ranged from 19 to 58 years, with a median of 43 and mean of 28±39.5 years. All of them were Asian. About 25.0% and 17.9% of them were over weight and obese according to a body mass index of 25.0-29.9 and 30.0 kg/m^2or greater, respectively. One third, 32.1% of them had abnormal but not clinically significant finding of electrocardiogram (ECG). Their medical conditions other than schizophrenia included 2 with hypertension, 1 insomnia, 1 Hyperlipidemia, and 1 ischemic stroke. Most of them, 89.3%, ever had episodes of schizophrenia prior to the screening visit. Duration of the illness ranged from 1 to 41 years with a median of 7 years. Majority of the patients, 85.7%, were schizophrenia with paranoid type, i.e., DSM Code of 295.3.

At the screening visit (during a period of 7 days prior to Day 1) which involved a total of 28 patients, their mean scores with the median and range of each neurological assessment were: 1) Modified Simpson-Angus Scale (MODIFIED SAS) of 2.1±3.5 (median: 0; range: 0-12); 2) Abnormal Involuntary Movement Scale (AIMS) of 1.2±3.5 (median: 0; range: 0-15); 3) Barnes Akathisia Rating Scale (BARS) of 0.6±1.3 (median: 0; range: 0-5); 4) Positive and Negative Syndrome Scale (PANSS) total score of 92.4±23.1 (median: 85.5; range: 67-154). Their Clinical Global Impression - Severity of Illness (CGI-S) were 53.6% moderately ill, 35.7% markedly ill, and 10.7% severely ill. By these, 24 patients met eligibility requirements and continued to be in the study.

Followings are summary of efficacy assessment score at Days 1 (n=24), 14 (n=21), and 42 (n=17), respectively. Number of patients at each visit was reduced due to exclusion of patients who did not meet eligibility requirements to continue to the subsequence visit. For each neurological assessment, there were 5 figures at each of the 3 visits which represent mean±SD, median, minimum and maximum score. For Modified Simpson-Angus Scale (MODIFIED SAS) score, it was 1.4±3.3 (median: 0; range: 0-13) at Day 1, 0.6±1.5 (median: 0; range: 0-6) at Day 14, and 0.7±1.2 (median: 0; range: 0-4) at Day 42.

For Abnormal Involuntary Movement Scale (AIMS) score, it was 0.6±2.4 (median: 0; range: 0-12) at Day 1, 0.1±0.3 (median: 0; range: 0-1) at Day 14, and 0.3±0.8 (median: 0; range: 0-3) at Day 42.

For Barnes Akathisia Rating Scale (BARS) score, it was 0.5±1.1 (median: 0; range: 0-4) at Day 1, 0.1±0.5 (median: 0; range: 0-2) at Day 14, and 0.1±0.3 (median: 0; range: 0-1) at Day 42.

For Positive and Negative Syndrome Scale (PANSS) total score, it was 85.3±28.8 (median: 79.5; range: 0-154) at Day 1, 49.0±34.1 (median: 63.0; range: 0-90) at Day 14, and 48.5±28.6 (median: 55.0; range: 0-108) at Day 42.

Summary score for each subscale of PANSS score were analyzed. For the Positive Scale of the PANSS score, it was 21.0±9.7 (median: 19.0; range: 0-39) at Day 1, 13.1±10.0 (median: 14.0; range: 0-30) at Day 14, and 11.9±7.5 (median: 11.0; range: 0-26) at Day 42. For the Negative Scale of the PANSS score, it was 23.4±7.8 (median: 23.0; range: 0-39) at Day 1, 12.1±8.7 (median: 14.0; range: 0-26) at Day 14, and 12.8±7.7 (median: 14.0; range: 0-27) at Day 42. For the General Psychopathology Scale of the PANSS score, it was 40.8±14.9 (median: 40; range: 0-76) at Day 1, 23.7±16.9 (median: 28.0; range: 0-46) at Day 14, and 23.9±14.7 (median: 27.0; range: 0-57) at Day 42.

For Clinical Global Impression - Severity of Illness (CGI-S) score, it was 4.6±0.7 (median: 4.0; range: 4-6) at Day 1, 3.2±1.1 (median: 3.0; range: 0-5) at Day 14, and 2.7±1.1 (median: 2.5; range: 1-5) at Day 42.

There were 13 patients reported experiencing at least one adverse events. Most common adverse events include headache, constipation, hypotension, and stiff nose. The former affected in 5 patients while the remaining occurred in 3 patients. None of these was reported to be severe.