AstraZeneca

STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: Seroquel IR
ACTIVE INGREDIENT: Quetiapine

Study No: NIS-NTW-SER-2008/1
A naturalistic observational study to evaluate efficacy of 2nd-generation antipsychotics and remission status for patients with schizophrenia / schizoaffective disorder

Developmental phase: Naturalistic observation
Study Completion Date: 27 Sep. 2010
Date of Report: 29 Mar. 2011

OBJECTIVES:

Primary objective:

- CGI-Severity of Illness (CGI-SI)

Secondary objective:

- CGI-Degree of change (CGI-DC)
- Montgomery and Asberg Depression Rating Scale (MADRS)
- Global Assessment of Functioning Scale (GAF)
- Remission status
- DIEPSS and other variables for patients' tolerability

METHODS:

This was a naturalistic, prospective, multi-centre observational study to explore efficacy of various 2nd-generation antipsychotic for acute management of, or improvement on those not-adequately controlled, Subjects who met the eligibility criteria were included in the study. The non-interventional study was designed to no 'randomization' assignment and exactly followed routine clinical practice. The assumption of recruited ratio between the quetiapine and non-quetiapine therapy was 1:1. Data were collected at enrollment and during routine visits occurring at Day 3, week 1, week 2 and week 4 if applicable. To screen patients not achieving remission at enrollment visit, 8-items of PANSS from criteria of Andresen working group was assessed, from which, definition of remission applied as "A score of mild or less ($\leqq$3) simultaneously on all 8 proposed PANSS items.

Status of remission was assessed again at end of evaluation period (week 4). CGI-SI for assessing clinical severity, MADRS for depression, GAF for functioning was evaluated upon enroll, and at day 3, week 1, week 2, and week 4. CGI-DC was assessed for each follow-up visit after enrollment. DIEPSS and BMI (including waist circumference) were recorded upon enroll and at each follow-up visit. During study period, acute episode or which rendered into hospitalization was recorded and documented.

RESULTS:

Patient dispositions:

A total of 491 subjects were enrolled in the study, where 134 subjects treated with quetiapine and 357 subjects treated with non-quetiapine. Of the total 491 enrolled patients, 16 patients (6 subjects in quetiapine group; 10 subjects in non-quetiapine group) did not have any post-baseline assessment and 1 subject (patient 11008) used risperidone and olanzapine simultaneously. These 17 subjects were excluded from intent-to-treat and per-protocol population. Thus, ITT population contained 474 subjects where 128 subjects treated with quetiapine and 346 subjects treated with non-quetiapine. There were 9 subjects (2 in quetiapine group and 7 in non-quetiapine group) who did not meet the inclusion criteria of age and 64 subjects achieved remission status at baseline (22 subjects treated with quetiapine and 42 patients treated with non-quetiapine). Therefore, PP population included 104 patients in quetiapine group and 297 patients in non-quetiapine group.

***Demographics*:**

For ITT population, the two treatment groups were well-balanced with respect to demographic characteristics, except for age and atypical antipsychotics. The average age was 41.2 years old of quetiapine group, ranging from 17.0 to 71.0 years old; of non-quetiapine group, average age was 38.0 years old, ranging from 13.0 to 81.0 years old. Subjects treated with quetiapine were statistically older than those treated with non-quetiapine with p-value=0.0069. The number of male/female was 59/69 in quetiapine group and 191/155 in non-quetiapine group. The mean weight and height of patients in this study were 67.9 kg and 163.2 cm in quetiapine group, and 69.0 kg quetiapine 163.5 cm in non-quetiapine group, respectively. The body mass index was 25.5 kg/m^2 of quetiapine group and 25.7 kg/m^2 in non-quetiapine group. Most common used baseline atypical psychotics of non-quetiapine group included risperidone (24.9%), aripiprazole (18.5%), and paliperidone (18.5%). The drug exposure of atypical antipsychotics indicated slightly increase of total daily dose from baseline to the end of study.

***Efficacy results*:**

Based on the analysis of efficacy, the primary efficacy of ITT population demonstrated there was a significant difference more than one point in mean overall CGI-SI score for both of the two treatment therapies. At baseline, the overall severity of CGI-SI score of observed data was 4.27 and 4.32 for quetiapine group and non-quetiapine group, respectively. After 4 weeks of treatment, CGI-SI of quetiapine group decreased to 3.25 and that of non-quetiapine group reduced to 3.26. The CGI-SI had a reduction of 1.06 for quetiapine group and 1.05 for non-quetiapine group. However, the difference between the two therapy groups did not statistically significant.

The overall severity of CGI-DC score at Week 4 was 2.97 score for quetiapine group and 3.09 for non-quetiapine group. These indicated minimally improvement was detected after 4 weeks of treatment.

The efficacy results of PP population were comparable to the results of ITT population. Though the effects of quetiapine were not significant different from non-quetiapine for other secondary efficacy parameters, such as MADRS, GAF, and remission status, quetiapine was still efficacious in these parameters. In addition, patients without remission at baseline indicated severe score of CGI-SI. Patients with lower CGI-SI also showed more improvement than patients with higher CGI-SI.

Safety results:

The safety profiles included DIEPSS and vital signs. DIEPSS total score for quetiapine group decreased from 4.45 at baseline to 1.84 at Week 4 and for non-quetiapine group changed from 4.04 at baseline to 2.42 at Week 4. Statistically more reduction in quetiapine group was detected at the end of study (quetiapine vs. non-quetiapine: -2.61 vs. -1.63). Similar results were also demonstrated by DIEPSS Parkinsonism score. As for treatment emergent Parkinsonism and akathisia were comparable between quetiapine and non-quetiapine group. With regard to vital signs, quetiapine group reported higher SBP at Week 1 and higher DBP at Week 1 and Week 4 than non-quetiapine group. Nevertheless, the differences were not clinically meaningful. In general, both atypical antipsychotic therapy groups were of no safety concern, and no clinically significant safety issues were identified.