AstraZeneca

STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: Seroquel
ACTIVE INGREDIENT: Quetiapine

Study No: NIS-NKR-SER-2007/1
Observational study to evaluate efficacy of Quetiapine Fumarate in patients with schizophrenia and schizoaffective disorder for 24 weeks spontaneously

Developmental phase: Marketed
Study Completion Date: 2008-05-31
Date of Report: 2009-01-22

OBJECTIVES:

The main objective of this study was to evaluate efficacy of Quetiapine in actual clinical practice for 24 weeks in patients with schizophrenia and schizoaffective disorder. Primary efficacy was analyzed respectively grouping into two group based on severity of initial symptom in treatment. In patients with CGI-S≥4, improvement rate was surveyed and in patients with CGI-S≤3, not worsening rate was researched.

In addition, items below were to be collected and assessed though this study.

- Change of psychiatric symptom using by CGI-5 factor scale.
- Response rate, aggravation rate and remission rate using by CGI-S scale
- Exploratory analysis of the relationship between pattern of Quetiapine dosage and result of treatment

METHODS:

In this study total 898 patients in 53 institutions were enrolled. Among these patients 38 patients were excluded because of violation of inclusion criteria and 39 patients due to not surveying CGI-S at visit 1 and CGI-I more than once so total 821 patients' data was used for analysis.

RESULTS:

1. Clinical Global Impression

At baseline, the mean CGI-S was 4.49 ± 1.08 and mean CGI-S was 2.76 ± 1.09 at last visit, so mean score of 1.73 ± 1.36 had been declined with statistic significance ($p < .0001$).

In CGI-I assessed at last visit, 'Much improved' was 275patients (41.48%) and was followed by 'Minimally improved' in 194 patients (29.26%) and 'Very much improved' in 125 patients (18.85%) respectively.

2. Efficacy Evaluation

i. Primary endpoint

The result of primary endpoint i.e. CGI-I score at the end of study was analyzed classified by baseline CGI-S (CGI-S≤3, CGI-S≥4). The results were as following.

At the end of study, overall improvement rate was evaluated by the rate of improved symptoms (CGI-I≤2) in patients with CGI-S≥4 at baseline and not worsening rate (CGI-I≤4) in patients with CGI-S≤3. The improved patients was 365(54.48%) in patients with CGI-S≥4 (initial severity more than moderate) and 148(98.01%) in patients with CGI-S≤3 (initial severity less than mild), so total 513 patients (62.48%) was evaluated as improved.

Among the patients with CGI-S≤3 at baseline, the mean treatment dose of Quetiapine in improved patients was 403.61± 235.34 mg and in not improved patients was 316.67 ± 104.08 mg. Among patients with CGI-S≥4 at baseline, the mean dose was 536.87 ± 217.86 mg in improved patients and 567.93±247.50 mg in not improved patients. This dose difference didn't show statistical significance.

ii. Secondary endpoint

1. Change of CGI-5 factors

In patients with positive symptom, the mean score of 1.80 ± 1.40 decreased from 4.27 ± 1.27 at baseline to 2.47 ± 1.13 after treatment and mean score of 0.94 ± 1.29 in patients with negative symptom, 1.00 ± 1.33 in depressive symptom, 1.01 ± 1.26 in cognitive symptom and 1.54 ± 1.52 in excitation symptom respectively. All 5 symptoms were declined with statistical significance ($p < .0001$).

2. Treatment response rate

Treatment response rate was evaluated in 670 patients with CGI-S≥4 at the beginning of treatment. The treatment response rate was defined as improvement of 2 and more in CGI-S in patients with CGI-S≥5 at the beginning of treatment and as improvement of 1 and more CGI-S in patients CGI-S=4 at the beginning of treatment.

Treatment response rate was 76.00% with improvement of 2 and more in CGI-S of 304 patients in 'CGI-S≥5' group and treatment response rate was 82.22% with improvement of 1 and more in CGI-S of 222 patients in 'CGI-S=4' group, so overall treatment response rate was 78.51%.

3. Worsening rate

The worsening rate was surveyed in 151 patients with less than mild (CGI-S≤3) symptom at baseline. The worsening of symptom was defined as increase by 2 or more than 2 in CGI-S. In case of CGI-S=1 at baseline, worsening was defined as increase by at least 3 or more than 3 in CGI-S.

As a result of analysis, there was no worsening patients in 'CGI-S=1' group and 4 patients(2.67%) out of 150 patients with CGI-S 2 or 3 were defined as worsened cases, so overall worsening rate of was 2.65%(4/147patients).

4. Remission rate

As result of remission rate defined as CGI-S≤3 for more than 2 consecutive months, remission was observed in 630 patients, so the overall remission rate was 76.74%.

5. Treatment effect

The result of treatment effect per each visit after visit 3 was as follows.

At visit 3 'Minimally improved' was 420 patients (53.23%) and 281 patients (35.61%) of 'Moderately improved', 46 patients(5.83%) of 'Very much improved' and 40 patients(5.07%) of 'No change or worse' was followed. At visit 6 'Moderately improved' was 331 patients (47.42%) and was followed by 186 patients (26.65%) of 'Minimally improved' and 160 patients (22.92%) of 'Very much improved'. At visit 8, 304 patients(45.65%) of 'Moderately improved' was followed by 231 patients(34.68%) of 'Very much improved' and 123 patients(18.47%) of 'Minimally improved'. Therefore increase number of visit lead to increase of improvement rate (Cochran-Mantel-Haenszel test, $p<.0001$).

6. Adverse Event

At visit 3, in 682 patients (90.33%) adverse event didn't occur. Among adverse events, adverse event not being remarkably harmful to patient's ability were 68 cases (9.01%) was and being remarkably harmful were 5 cases (0.66%). At visit 8, the number of patients without adverse event was 632(96.19%), 23 adverse events (3.50%) was reported as not remarkably harmful to patient's ability and 2 adverse events (0.30%) was remarkably harmful. There were no adverse events exceeding the benefits of treatment in every visit.

7. Drop out

As a result of analyzing the reason of dropout 151 patients, the failure of follow-up was 53 patients (6.18%) and followed by the 42 patients (4.90%) of no effect or withdrawal of informed consent and 19 patients (2.21%) of low compliance.

In analysis of dropout reason per visit, in 1 patient whose last visit was visit 1, reason was no effect or withdrawal of consent. In 28 patients whose last visit was visit 2, main dropout reason was follow-up loss (12 patients). Among 35 patients whose third visit was last visit, main reason was no effect or withdrawal of consent in 14 patients. Among 31 patients whose 4^{th} visit was last visit, main reason was other reason (11 patients). Follow up loss was main dropout reason in 12 patients out of 27 patients whose 5^{th} visit was last visit, 7 patients out of 19 patients whose 6^{th} visit was last visit and 6 patients out of 10 patients whose 7^{th} visit was last visit respectively.