STUDY REPORT SUMMARY : SERENITY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: Not applicable, (Non-interventional trial, i.e. therapy according to current practice.)

ACTIVE INGREDIENT:

Study No: SRP-NB-SER-2006/1
SERENITY: Evaluating the effectiveness of atypical antipsychotics in the community – a prospective, multicentre, observational study to evaluate the impact on Quality of Life of GP-based management of antipsychotic treatment in Belgium.

Developmental phase: NIS

Study Completion Date: 14 AUG 2008

Date of Report: 17 April 2009

OBJECTIVES:

This SRP was performed to study the effectiveness of atypical antipsychotics as defined by the 3 domains: functioning, efficacy and tolerability.

Unlike many other branches of medicine, the field of psychiatry in general lacks laboratory or other biologic measures that can be used to assess the presence or severity of illness. To more objectively define various types of mental illness and to standardize assessment of these disorders, mental health practitioners have developed a wide array of rating scales for psychiatric illness that can be utilized in a variety of settings. The scales used for this study were selected because of their appropriateness in this GP setting.

The primary objective for this study was to evaluate the patient's functioning, by measuring the Quality of Life. Quality of Life was assessed by the Q-LES-Q-16 (PRO).

Secondary objectives were to evaluate

- The clinical efficacy and tolerability of atypical antipsychotics, as assessed by the Clinical Global Impression (CGI) and Patient Global Impression of Change (PGIC) scores.

The wellbeing of the patients taking atypical antipsychotics, as assessed by the Sheehan Disability Scale (SDS).

METHODS:

This observational study is a non-interventional study, which required no additional or monitoring procedures other than the ones applied with current medical practice. Patients diagnosed with Schizophrenia or Bipolar Disorder (currently in a manic episode) and for whom the GP decided to prescribe an atypical antipsychotic in accordance with the Summary of Product Characteristics (SPC) and current medical practice were included in this SRP.

Demographics, patient selection criteria, psychiatric medical history, and current medical condition were assessed only at Visit 1 (day 0). Additional psychotropic drugs, name and dose of atypical antipsychotic, Q-LES-Q-16, SDS, and CGI were assessed at Visit 1 (day 0), at Visit 2 (after 4 ± 2 weeks), and at Visit 3 (after 8 ± 2 weeks).

Number of Patients (Planned and Analysed)

Planned: 250 patients

Enrolled: 252 patients

Analysed for safety: 252 patients

Analysed for efficacy: 244 (Full Analysis), 223 (Per Protocol)

Completed: 226 patients

The premature withdrawal was not documented for 1 of the 26 patients not completing the SRP. Reasons for withdrawal were non-compliance (14), adverse events (6), lack of efficacy (3), and withdrawal of consent (1). The reason for 1 patient was missing.

Main Criteria for Inclusion

Patients diagnosed with Schizophrenia or Bipolar Disorder (currently in a manic episode) and for whom the GP decided to prescribe an atypical antipsychotic in accordance with the SPC and current medical practice were eligible for inclusion. Patients had to be between 18 and 65 years old and voluntarily sign informed consent.

If the patient was female, she was obliged to use a reliable method of contraception as stated in the Summary of Product Characteristics of atypical antipsychotics.

Study Drug, Dose and Mode of Administration

Atypical antipsychotics were used according the SPC and the current medical practice. Additional psychotropic medication was recorded at each visit.

Duration of Treatment

The patients were followed during 8 ± 2 weeks, with 3 visits in total:

Visit *1* (enrolment); Visit 2 (4 ± 2 weeks after Visit 1); Visit 3 (final visit 8 ± 2 weeks after Visit 1).

A monthly visit to the GP was considered common medical practice for this population. Therefore, the visit schedule with ± 2 weeks visit-windows was designed be in line with this common daily practice.

Criteria for Evaluation – Efficacy

The following criteria for evaluation of efficacy and tolerability were used: CGI and PGIC. The Quality of Life was assessed by the Q-LES-Q-16 (PRO), the wellbeing of the patients by the SDS.

Criteria for Evaluation – Safety

Due to the non-interventional character of a Scientific Research Program, no pro-active safety data collection took place. Only spontaneously mentioned safety events had to be reported as required by the post-marketing pharmacovigilance regulations.

Statistical Methods

Descriptive statistics were calculated for this non-interventional study, including 95% confidence intervals (CIs).

Descriptive statistics for a specific variable were displayed for combinations of visits, and (possibly) analysis populations, and analysis types (OC, LOCF).

Descriptive statistics for continuous variables were the number of non missing observations, the number of missing observations, arithmetic mean, standard deviation, median, minimum and maximum, and confidence intervals if applicable.

Descriptive statistics for categorical or dichotomous variables were the frequencies and percentages.

The efficacy was assessed by studying the confidence intervals for:

1. The Q-LES-Q summary score (change from baseline) (at visit 2 and 3).
2. The proportion of patients, for which an improvement on the PGIC was indicated,
3. The effect size was calculated from the Q-LES-Q summary scores in the following way: defined as a score of 1, 2, or 3 (at visit 2 and 3).

The proportion of patients, for which an improvement on the CGI-I was indicated, defined as a score of 1, 2, or 3 (at visit 2 and 3).

Effect size 1: Q-LES-Q mean change from baseline divided by baseline STD.

Effect size 2: Q-LES-Q mean change from baseline divided by STD of differences.

The improvement of well-being was assessed by studying the confidence intervals and shift tables of the Sheenan Disability Scale variables.

The efficacy and the tolerability were assessed by studying the PGIC, CGI-I and CGI-S shift tables and improvement confidence intervals.

The primary and secondary efficacy analysis was repeated for the subgroup SEROQUEL, defined as the patients for whom Seroquel was described at visit 1 and who did not change to other antipsychotic medication at Visit 2.

Additionally, the relationship between the satisfaction with the medication on the one hand (Q-LES-Q item 15) and the clinical efficacy, the tolerability and the patients' well-being were analysed by calculating the Pearson correlation coefficient and carrying out categorical analyses (ANOVA and Chi-square).

RESULTS:

This study showed an improvement in the patients' functioning after the start of atypical antipsychotics in patients diagnosed with either Schizophrenia or a manic episode of a Bipolar Disorder (Visit 3: Q-LES-Q mean change from baseline 24.62, 95% CI 21.70 – 27.55; Q-LES-Q effect size 1 1.21; Q-LES-Q effect size 2 1.12).

This study showed an improvement in the patients' well-being between Baseline and Follow-up. The SDS total score decreased substantially between Baseline and Follow-up (mean change at Visit 3: -9.26;
CI: -10.68 – -7.84). The number of days lost and the number of unproductive days at work or school decreased between Baseline and Follow-up (mean change at Visit 3: days lost: -1.88, CI: -2.26 – -1.51; unproductive days: -2.31, CI: -2.68 – -2.93).

The assessments on efficacy and tolerability were positive. The CGI-S scores decreased between Baseline and Follow-up (mean change at Visit 3: -1.92; CI: -2.14 – -1.70). Also the CGI-I scores and the PGIC scores decreased between Baseline and Follow-up, indicating that the patients' condition improved (mean value at Visit 3: CGI-I: 2.16, CI: 2.01 – 2.32; PGIC: 2.27, CI: 2.11 – 2.43).

A positive relationship was observed between the medication satisfaction on the one hand and the efficacy, the tolerability and the patient's well-being on the other hand.