AstraZeneca

Non-Interventional Study (NIS) Report Synopsis

NIS Name/Code	RECONNECT-S GAMMA/NIS-NME-SER-2011/1
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RECONNECT-S GAMMA: A non-interventional study to observe real-life usage of atypical antipsychotics in the acute inpatient management of schizophrenia

Study dates:	**First Subject In:** 19 December 2011 **Last Subject Last Visit:** 31 May 2012

NIS REPORT SYNOPSIS

RECONNECT-S GAMMA: A non-interventional study to observe real-life usage of atypical antipsychotics in the acute inpatient management of schizophrenia

Participating Countries: Study centers in Hungary, Latvia, and Romania.	
Investigators: In order to ensure that the study represented real-life clinical practice, representative study centers (i.e. Primary Care centers, Hospitals and Specialists centers) that managed the defined patient population in each participating country were identified and selected. A total of 33 psychiatrists participated: 8 in Hungary, 10 in Latvia, and 15 in Romania.	
Number of Subjects (planned and analyzed): Planned: 500; Actual: 496; Completed: 496	
Publications (reference): No publications have been completed at the time of the final study report approval.	
Studied Period: First Subject In: 19 December 2011 Last Subject Last Visit: 31 May 2012	**Phase of Development**: Not applicable

Objectives:

Primary objective: The primary objective of this Non-Interventional Study (NIS) was to describe the use of atypical antipsychotics in subjects with schizophrenia during the hospitalization due to an acute psychotic episode by evaluation of drug, dose, and mode of administration of the medication.

Secondary objectives:

- To evaluate the treatment practice of atypical antipsychotics as monotherapy during the hospitalization period
- To evaluate the treatment practice of combinations of antipsychotics during the hospitalization period
- To investigate the main criteria used for selection of an antipsychotic to treat an acute episode of schizophrenia
- To describe the use of psychometric scales to evaluate the disease symptoms during the hospitalization period
- To investigate the use of concomitant psychiatric medication (other than atypical antipsychotic) during the hospitalization
- To investigate the relationships between atypical antipsychotic medication used during the hospitalization and maintenance therapy recommended upon discharge

Methods: This was a non-interventional, multinational, multicenter study to describe the management of subjects with schizophrenia who were hospitalized due to an acute psychotic episode. An NIS is a study in which no

additional diagnostic or monitoring procedures is applied to the subjects, other than the day-to-day practice. During the study, the subjects conducted 1 visit on the day of their discharge after hospitalization due to an acute psychotic episode. Information from the subjects was collected during 1 single visit, performed on the day of subject discharge. On the study visit, data on demographics, diagnosis, and medical history were recorded. Data on antipsychotic treatment and concomitant medication were collected for the hospitalization period and the recommendation at discharge. All subject data were coded, processed, and analyzed by the medical department of AZ or a company representing AZ. Results of the study were presented to the participating investigators.

Diagnosis and Main Criteria for Inclusion: Subjects with schizophrenia who were hospitalized due to an acute psychotic episode were recruited to this study on their day of discharge from the hospital.

Male and female subjects were included in this study if they were 18 years or older, provided written informed consent, met the diagnostic criteria for schizophrenia stated in The Diagnostic and Statistical Manual of Mental Disorders, was hospitalized due to an acute psychotic episode and had the ability to understand and comply with the requirements of the study, as judged by the investigator.

Subjects were not included if they were participating in any clinical trial at the time of enrolment, or had previously enrolled in the present NIS (i.e., in case there was occurrence of a subject being re-enrolled during the enrolment period).

The prescription of any medicinal product was clearly separated from the decision to include the subject in the NIS.

Duration of Follow-up: There was no follow-up period. Subjects had 1 visit on the day of their discharge after hospitalization.

Test Product, Dose, Mode of Administration, and Batch Number(s): Not applicable.

Reference Therapy, Dose, Mode of Administration, and Batch Number(s): Not applicable.

Criteria for Evaluation

The composite variable consisted of the following:

- Used atypical antipsychotic(s) during hospitalization
- Daily dose of atypical antipsychotic(s) during hospitalization
- Mode of administration of atypical antipsychotic(s) during hospitalization

The data for the primary variable were collected by review of hospital records of the current hospitalization. Start date, stop date/on-going, reason for treatment, dose, total daily dose, and reason for change of treatment (if applicable) were registered for all subjects during the hospitalization period. The primary objective of the study was analyzed by calculating the percentage of subjects using atypical antipsychotic treatments during hospitalization. This was summarized by country and overall. Also summarized was the highest daily dose for each subject and its mode of administration.

Safety: Because of the non-interventional character of this study, no safety data were proactively collected.

Exploratory variables were demographic, educational, economic, social, psychiatric and somatic health data which were collected to describe the study population.

Statistical Methods:

A NIS is a study in which epidemiological methods, including other methods, are used to analyze human population health data. A descriptive analysis approach (including frequency tables) was used. As appropriate, a two-sided 95% confidence interval was obtained for the population estimation of the variables. All calculations and summaries were produced using SAS Version 9.2 (SAS 2009). Medications were coded using the WHO drug dictionary, version 12.1.

The data was summarized in tabular form using the analysis population. The summaries were presented by country and overall. Listings were tabulated and sorted by site and subject number. For continuous parameters, the mean, standard deviation (SD), 95% confidence interval for the mean, median, lower/upper quartile, minimum and maximum values were provided. For categorical parameters, the frequency and percentage of subjects in each category will be provided.

Subjects who met the diagnostic criteria for schizophrenia stated in the DSM-IV and were hospitalized due to an acute psychotic episode were enrolled in the study. A total of 496 subjects were enrolled: 183 in Hungary, 102 in Latvia, and 211 in Romania. Of these subjects, all 496 were included in the statistical analysis.

Results

Demographics and Baseline Characteristics:

Of the 496 study subjects, 243 (49.0%) were male and 253 (51.0%) were female. The mean age ± SD of the subjects was 43.5 ± 11.58. All subjects were Caucasian (race data missing for 1 subject) and the mean number of years of education ± SD was 11.6 ± 2.64. The majority of subjects were on sickness pension (61.7%), unemployed (13.1%), or retired (10.7%). Over 40% of the subjects reported have psychosocial problems and approximately 8% of the subjects had made 1 or more suicide attempts.

Main Results:

The primary objective of this NIS was to describe the use of atypical antipsychotics in subjects with schizophrenia during the hospitalization due to an acute psychotic episode by evaluation of drug, dose, and mode of administration of the medication. Of the 479 subjects (96.6%) treated with atypical antipsychotics, the most frequently used medications were quetiapine (n=129; 27.4%), oral risperidone (n=95; 20.2%), oral olanzapine (n=104; 22.1%), and clozapine (n=73; 15.5%). The overall average (mean) daily dose ± S.D. was 601.7 ± 219.51 mg for quetiapine (dose range can be from 200 to 800 mg/day), 4.7 ± 1.93 mg for oral risperidone (dose range can be from 4 to 6 mg/day with a maximum of 16 mg/day), 16.2 ± 5.96 mg for oral olanzapine (dose range can be from 5 to 20 mg/day), and 233.9 ± 171.86 mg for clozapine (dose range can be from 200 to 900 mg/day). A smaller percentage of subjects received risperidone and olanzapine intramuscularly (n=28; 6.0% and n= 9; 1.9%, respectively). The average daily dose for oral risperidone was highest for Latvia and lowest for Hungary. The average daily dose for oral olanzapine was highest for Hungary and lowest for Romania.

Among the 496 subjects, 479 (96.6%) were treated with at least 1 AAP medication, 14 (2.8%) were not treated with AAP medications (ie, they received an AP and other medication together), and 3 (0.6%) received something other than an antipsychotic medication such as anxiolytics or antidepressants. Of the subjects treated with atypical antipsychotics, 49 subjects (9.9%) were treated with a single atypical antipsychotic as monotherapy and 12 subjects (2.4%) were treated with more than 1 atypical antipsychotic. Only 1 subject (0.2%) was treated with a typical antipsychotic as monotherapy.

A total of 418 subjects (84.3%) were treated with atypical antipsychotics in combination with other psychiatric medications: 20 (4.0%) with a combination of atypical and typical antipsychotics, 307 (61.9%) with an atypical antipsychotic and another medication, and 91 (18.3%) with a typical antipsychotic and another medication.

Medication history (41.9%), current symptoms (43.8%), or preference on personal clinical experience (29.0%) were reported most frequently as the rationale in selecting atypical antipsychotic treatment. Clinical experience of the doctor was reported as the method of evaluation for 93.3% of the subjects. Psychometric scales were not used to evaluate the disease symptoms during the hospitalization period for any of the subjects.

During the study, 435 subjects (87.7%) were treated with at least 1 concomitant psychiatric medication. Of these, 267 (53.8%) were treated with antiepileptics, 180 (36.3%) with anxiolytics, 125 (25.2%) with antipsychotics, and 101 (20.4%) with antidepressants.

The overall mean ± SD number of days the subjects were hospitalized was 28 ± 36.99. By country mean hospitalization days were 37 ± 14.05 for Latvia, 31.3 ± 48.82 for Hungary, and 22.6 ± 31.44 for Romania. Upon discharge, a significant number of subjects (n=373; 75.2%) were prescribed atypical antipsychotics as maintenance therapy. Of the number of subjects treated with AAP during hospitalization, 335 (69.9%) were prescribed the same medications at discharge that they had been treated with during hospitalization. The prescription pattern of atypical antipsychotic drugs for maintenance therapy upon discharge was different for Hungary (52.5%) compared to Latvia (99.0%) and Romania (83.4%).

Safety Results:

Due to the non-interventional character of this study, no pro-active safety data collection took place. Only spontaneously mentioned safety events were reported as required by the post-marketing pharmacovigilance regulations.

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