



---

**Non-Interventional Study (NIS) Report**

NIS Name	RECONNECT-S BETA
NIS Code	NIS-NME-XXX-2011/1
Edition Number	Final
Date	16 December 2013

---

---

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

---

---

**Study dates:** 7 April 2012 to 31 December 2012**First Subject In:** 7 April 2012**Last Subject Last Visit:** 31 December 2012

---

This submission / document contains trade secrets and confidential commercial information, disclosure of which is prohibited without providing advance notice to AstraZeneca and opportunity to object

Associated Document: T15 NIS Report (NISR),

Template Active Date: May 20102

Parent SOP: LDMS\_001\_000912618-P85-1-X Planning, Approval, Conduct and Reporting of Non-Interventional Studies (NISs)

## NIS REPORT SYNOPSIS

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

<b>Participating countries:</b> Egypt, Saudi Arabia, Gulf States (includes Kuwait and United Arab Emirates).	
<b>Number of subjects (planned and analysed):</b> 1050 planned, 1076 enrolled, 1057 analysed.	
<b>Publications (reference):</b> No publications have been completed at the time of the final study report approval.	
<b>Studied period:</b> First subject in: 7 April 2012  Last subject last visit: 31 December 2012	<b>Phase of development:</b> Not applicable
<b>Objectives:</b> The primary objective of this non-interventional study (NIS) was to describe the use of atypical antipsychotics in subjects with schizophrenia during hospitalization due to an acute episode by evaluation of drug, dose, and mode of administration of the medication.  Secondary objectives of the study were: <ul style="list-style-type: none"><li>• To evaluate use of atypical antipsychotics as monotherapy during the hospitalization period.</li><li>• To evaluate use of combinations of antipsychotics during the hospitalization period.</li><li>• To investigate the main criteria used for selection of an antipsychotic to treat an acute episode of schizophrenia.</li><li>• To describe the use of psychometric scales to evaluate the disease symptoms during the hospitalization period.</li><li>• To investigate the use of concomitant psychiatric medication (other than atypical antipsychotics) during the hospitalization period.</li><li>• To investigate the relationship between atypical antipsychotic medication used during the hospitalization and maintenance therapy recommended upon discharge.</li></ul>	

**Methods:**

This was a non-interventional, multicenter study to observe the management of subjects with schizophrenia who were hospitalized due to an acute psychotic episode. Subjects were managed per normal clinical practice until discharge. During the study, subjects participated in 1 visit on the day of their discharge after hospitalization due to an acute psychotic episode.

An NIS is a study in which no additional diagnostic or monitoring procedures are applied to subjects, other than the day-to-day practice.

**Diagnosis and main criteria for inclusion:**

This study included male or female subjects 18 years of age or older who met the Diagnostic and Statistical Manual of Mental Disorders, Text Revision, 4<sup>th</sup> Edition, criteria for schizophrenia, and were hospitalized for an acute psychiatric episode.

**Duration of follow up:**

Not applicable.

**Test product, dose, mode of administration, and batch number(s):**

Not applicable.

**Criteria for evaluation:**

The following variables were used to describe the primary objective:

- Used atypical antipsychotics during hospitalization
- Daily dosage of atypical antipsychotics during hospitalization
- Mode of administration of atypical antipsychotics during hospitalization

Secondary variables included the following:

- Percentage of subjects using atypical antipsychotics as monotherapy during the hospitalization period.
- Percentage of subjects using combinations of antipsychotics during the hospitalization period.
- Main criteria (subject's medication history, current symptoms and co-occurring conditions, other concurrent treatments, and preferences) used for selection of an antipsychotic during hospitalization, expressed as percentage.
- Percentage of subjects in whom psychometric scales were used to evaluate the disease symptoms during the hospitalization.
- Use of concomitant psychiatric medication (other than an atypical antipsychotic) during the hospitalization. Start date, stop date/ongoing, reason for treatment, highest

prescribed dose, route, and reason for change of treatment (if applicable) for all concomitant medications that the subjects had during the hospitalization period were collected.

- Correlation between antipsychotic medication used during the hospitalization and maintenance therapy recommended upon discharge.

#### **Statistical methods:**

An NIS uses epidemiological data and other methods to analyze human population health data.

A comprehensive Statistical Analysis Plan was prepared before database lock.

All statistical analyses were performed by Worldwide Clinical Trials under the direction of AstraZeneca Study Coordination Office by means of the SAS<sup>®</sup> statistical software system (SAS Institute, Inc., Cary, NC, USA).

A descriptive analysis approach (including frequency tables) was used to assess the outcome variables described. If appropriate, a 2-sided 95% confidence interval (CI) was obtained for the population estimation of the variables. All calculations and summaries were produced using SAS Version 9.3. Medications were coded using the World Health Organisation Drug Dictionary, version 12.1.

The data were summarized in tabular form using the analysis population. The summaries were presented by country and overall. Listings were also tabulated and sorted by site and subject number.

For continuous parameters, the mean, standard deviation (SD), 95% CI for the mean (where appropriate), median, minimum, and maximum values were provided.

For categorical parameters, the frequency and percentage of subjects in each category were provided.

#### **Results:**

##### Demographic and Baseline Characteristics

This NIS enrolled subjects with schizophrenia who were hospitalized due to an acute psychotic episode and who were recruited to this study on their day of discharge from the hospital. The analysis population included 1057 subjects: 480 from Egypt, 333 from Saudi Arabia, and 244 from the Gulf States.

The majority of subjects (74.9%) were male with a median age of 32 years; otherwise, the population was ethnically diverse, with many differences among countries. Subjects in Egypt were slightly more educated than subjects in Saudi Arabia and the Gulf States. Unemployment rates were near or above 50% in this subject population with schizophrenia.

The majority of subjects were single and lived with their parents. Approximately half of the

subjects had a history of psychosocial problems; 19.3% of subjects had been diagnosed with comorbid psychiatric conditions (with primary diagnosis of schizophrenia). The most frequently reported somatic concomitant illnesses were diabetes mellitus, hypertensive diseases, and other endocrine, nutritional, and metabolic diseases.

Overall, 45.8% of subjects had used antipsychotic medications in the month prior to hospitalization, with a lower percentage in Egypt compared with the other countries. Risperidone was the most frequently used prior antipsychotic medication overall.

### Main Results

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

More than 95% of subjects received treatment with atypical antipsychotics during hospitalization, and almost all medication was orally administered; however, atypical antipsychotic use was not an entrance criterion in this study. The mean hospital duration was shorter in Egypt (27.0 days [95% CI 25.0, 29.0]) compared with Saudi Arabia (41.5 days [95% CI 36.5, 46.4]) and the Gulf States (34.0 days [95% CI 29.7, 38.3]).

In Egypt, the most frequently administered antipsychotics were risperidone followed by clozapine, quetiapine, and olanzapine. In Saudi Arabia and the Gulf States, the most frequently administered antipsychotics were olanzapine and risperidone. The median orally administered risperidone dose was higher (6.0 mg) for subjects in Egypt compared with Saudi Arabia (4.0 mg) and the Gulf States (3.5 mg). The same was true for orally administered olanzapine (median dose of 20.0 mg in Egypt vs. 17.5 mg in Saudi Arabia and 15.0 mg in the Gulf States).

Only 17% of subjects were treated with an atypical antipsychotic drug as monotherapy. Combination treatment was common in all countries with more than half of the subjects receiving atypical antipsychotics in combination with other antipsychotic medications. In Egypt, the most frequent combinations were atypical antipsychotics with other antipsychotics (29.0%) and atypical antipsychotics with other antipsychotics and another class of medication (24.0). In Saudi Arabia and the Gulf States, the most frequently used combination (26.1% and 48.8%, respectively) was use of atypical antipsychotics with other medications.

The category of current symptoms was selected as the most frequent reason (62.2%) for selecting a particular treatment followed by medication history (26.5%) and preference based on personal experience (20.4%). In the Gulf States, the most frequently reported reason for treatment selection was preference based on personal clinical experience (47.1%). Atypical antipsychotic medication was prescribed as maintenance therapy to the majority of subjects (93.9%). The majority of the time (84.8%) the same atypical antipsychotic medication administered during hospitalization was prescribed at discharge. The correlation coefficient for the proportion of antipsychotic medications recommended as maintenance therapy was significant for subjects in Egypt (0.28;  $p < 0.001$ ) and subjects overall (0.21;  $p < 0.001$ ) but

not for subjects in Saudi Arabia (-0.02; p = 0.634) and the Gulf States (0.08; p = 0.129).

#### 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.

#### **In Summary:**

Overall, subjects in Egypt received higher mean doses of antipsychotics and had shorter mean hospital stays compared with subjects in Saudi Arabia and the Gulf States. They also had more frequent additional therapies, specifically electroconvulsive therapy and psychological treatment. There was a significant correlation coefficient for the proportion of antipsychotics recommended as maintenance therapy for subjects in Egypt.

Subjects in Saudi Arabia and the Gulf States had a lower use of non-atypical antipsychotics compared with Egypt; however, these subjects in these countries were more likely to receive therapies in other classes for the treatment of psychosis, specifically antiepileptic and anticholinergic therapies.

The main reported treatment evaluation method was clinical experience of doctor. Very limited use of psychometric scales to document treatment effectiveness was recorded.

In summary, this study indicated that the majority of subjects with schizophrenia were treated with atypical antipsychotics for acute psychotic episodes during hospitalization. Atypical antipsychotics were commonly used in combination with other psychiatric medications, rather than as monotherapy. The results of this study concurred with evidence from other observational studies showing that combinations are frequently used in clinical practice, inconsistent with current guidelines recommendations.

A number of inter-country differences in treatment practices were observed among the countries included in the study.

**Date of report:** 16 December 2013