Non-Interventional Study (NIS) Report	
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A non-intErventional, prospecTive, Open-label Study for the evaluation of the selection and outcome of the antipsychotic treatment switch in outpatients with schizophrenia (ETOS)

Study dates:	**First Subject In:** October 6th 2009 **Last Subject Last Visit:** September 30th 2010

NIS REPORT SYNOPSIS

A non-interventional, prospective, open-label study for the evaluation of the outcome of antipsychotic treatment switch in outpatients with schizophrenia (ETOS) as well as for the documentation of the reasons for the switch and the therapeutic management options.

Purpose: The main purpose of this study was to assess the outcome of a switch in antipsychotic treatment in schizophrenic patients. The study also documented in detail the reasons leading physicians to decide to proceed in switching antipsychotic treatment, as well as the therapeutic treatment options.

Methodology: This was an open-label, prospective, observational study.

Number of study sites & subjects: A total of 87 sites participated in the present study. Ten study sites were public hospitals and the remaining 77 sites were private healthcare clinics. A total number of 574 subjects were enrolled onto the study. However, the statistical analysis was performed on the Per Protocol Population (568 subjects).

Study Population:

The target population consisted of psychiatric outpatients diagnosed with schizophrenia which were treated at hospital outpatient clinics or private physicians' offices and had initiated a new antipsychotic treatment within two weeks before entry into the study.

Inclusion criteria:

- Outpatients, male and female, aged 18 to 65 years
- Diagnosis of schizophrenia (as per DSM-IV), at least 6 months prior to enrolment in the study
- Subjects who have initiated a new antipsychotic treatment within the preceding 2 weeks
- Subjects whose prior and current antipsychotic treatment consists of any typical or atypical antipsychotic monotherapy
- Subjects who are able and willing to participate in the study after having provided their written informed consent

Exclusion criteria:

- Subjects fulfilling criteria for diagnosis of any other psychiatric condition (except from schizophrenia), as per DSM-IV Axis I, concomitant organic mental disorder or mental retardation
- Substance abuse or dependence (with the exception of nicotine dependence), as defined by DSM-IV criteria and not in full remission
- Female subjects who are pregnant or lactating
- Participation in another study

Investigational and reference treatments: The study was conducted within the context

of common medical practice. This study was a non-interventional one and did not involve a treatment protocol or a clinic visit schedule. Subjects received approved therapy, at the discretion of their treating physician.

Objectives:

Primary:

- The evaluation of the outcome of treatment switch defined as an improvement in CGI-CB scale (Clinical Global Impression – Clinical Benefit)

Secondary:

- The documentation of the reasons leading physicians to antipsychotic treatment switch
- The documentation of therapeutic management options

LIST OF ABBREVIATIONS AND DEFINITIONS

ADR	Adverse Drug Reaction
AE	Adverse Event
BARS	Brief Adherence Rating Scale
CGI-CB	Clinical Global Impression-Clinical Benefit
CGI-I	Clinical Global Impression-Improvement
CGI-S	Clinical Global Impression-Severity
CI	Confidence Interval
CRF	Case Report Form
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders – 4th Edition
ΕΟΦ	Greek National Organization of Medicines
GCP	Good Clinical Practice
ICF	Informed Consent Form
ICH	International Conference on Harmonization
ITT	Intention-To-Treat
NA	Not Applicable
PANSS	Positive And Negative Syndrome Scale
SAS	Simpson-Angus Scale
SPC	Summary of Product Characteristics

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1. STUDY SITES

A total of 87 sites participated in this study. Ten study sites were public hospitals and the remaining 77 sites were private healthcare clinics. A complete list of the names of all participating sites and principal investigators can be found in Appendix B.

2. PUBLICATIONS

There are currently no publications disclosing the results of this study.

3. STUDY DATES

First Subject In: **06 October 2009**
Last Subject Last Visit: **30 September 2010**

This study was approved by the Scientific Committee/Administrative Council (IRBs) of the participating hospitals, as well as by the Greek National Organization of Medicines (ΕΟΦ).

4. BACKGROUND AND RATIONALE

Schizophrenia is a serious psychiatric disease, characterized by progressive disorganization of subject personality, with substantial impact on functionality and quality of life [1-3]. Besides the chronicity of its course, schizophrenia is accompanied by a lifelong suicide rate of 5 to 13% [4]. Therefore, the need for effective treatment of this disorder remains imperative.

The introduction of atypical antipsychotics in psychiatric practice has contributed to the more effective control of schizophrenic symptoms, thus achieving significant clinical benefit for the patient [5], while, at the same time, expectations towards improved subjects' compliance with administered treatment are raised [6-8]. Nonetheless, subsequent studies did not confirmed these expectations at the anticipated level [9,10].

In schizophrenic patients under antipsychotic treatment, high rates of treatment discontinuations and frequent treatment changes are quite common [11], as it is generally accepted that subjects who are not responding to an agent belonging to a particular class of psychotropic drugs or experience adverse events may show a better response to another substance of the same or another therapeutic class [12]. Various studies have indicated that subjects change their treatment with atypical antipsychotics at least twice a year (mean = 2.1, range = 0-7) [11].

The two more common reasons for switching antipsychotic treatment are lack of efficacy and occurrence of adverse events. Usually, the preferred time periods for a switch in antipsychotic treatment are during hospitalization for a relapse, during outpatient care when the patient is controlled and adequately socially supported, or when the patient himself is requesting the treatment switch [13,14].

Treatment switch is commonly performed from a typical to an atypical antipsychotic agent or from an atypical to another atypical antipsychotic. The reasons leading to the decision for a treatment switch as well as the therapeutic options for the management of each different case vary. The thorough dosage adjustment and the proper selection of the treatment may reduce both the rate of treatment discontinuations and the unnecessary changes, thus achieving better clinical outcomes [11].

Nonetheless, the question regarding whether a switch in antipsychotic treatment improves or not patients' outcome still remains unanswered, and is probably related to the therapeutic choice made each time [12]. This study aimed to document the reasons, the therapeutic options and the outcomes of switches in antipsychotic treatments, under normal clinical practice conditions, and at contributing to physicians' efforts for optimal treatment choice by providing additional scientific data.

The main purpose of this study was to evaluate the outcome of the switch in antipsychotic treatment in schizophrenic patients. The study also documented the detailed reasons leading physicians to decide to proceed in switching antipsychotic treatment, as well as the therapeutic management options.

5. OBJECTIVES

The primary study objective was:

- To evaluate the outcome of treatment switch defined as an improvement in CGI-CB scale (Clinical Global Impression – Clinical Benefit)

The secondary study objectives were:

- To document the reasons leading physicians to the switch in antipsychotic treatment
- To document the treatment options

6. STUDY DESIGN AND SELECTION CRITERIA

This was an observational study in which subjects, who had switched from their prior antipsychotic medication to any new antipsychotic treatment, were eligible to participate.

The study included outpatients recruited by both hospital sites and private physicians. The follow-up period for each participating subject was planned to last 4.5 months.

The study enrolled outpatients diagnosed with schizophrenia (as per DSM-IV), whose treating physician had recently switched their therapeutic treatment. As this was an observational study, no treatment protocol was applicable. The treatment administered to the participating subjects was determined according to the approved drug labels, at the physicians' discretion. The study was conducted under real life clinical practice conditions.

Inclusion criteria

- Outpatients, male and female, aged 18 to 65 years
- Diagnosis of schizophrenia (as per DSM-IV), at least 6 months prior to the enrolment into

the study

- Subjects who had initiated a new antipsychotic treatment within the preceding 2 weeks
- Subjects whose prior and current antipsychotic treatment consists of any typical or atypical antipsychotic monotherapy
- Subjects who are able and willing to participate in the study after having provided their written informed consent.

Exclusion criteria

- Subjects fulfilling the criteria for diagnosis of any other psychiatric condition (except from schizophrenia), as per DSM-IV Axis I, concomitant organic mental disorder or mental retardation
- Substance abuse or dependence (with the exception of nicotine dependence), as defined by DSM-IV criteria and not in full remission
- Female subjects who are pregnant or lactating
- Participation in another study

Table A: Study Flow Chart

	Baseline (Day 0)	Follow-up Period*		
		Week 6	Week 12	Week 18
Signed written consent	√			
Inclusion/exclusion criteria	√			
Enrolment	√			
Demographic data	√			
Somatometric data	√			√
Medical history	√			
Laboratory assessments**	√	√	√	√
PANSS Score***	√	√	√	√
CGI-S Score	√			√
CGI-I Score		√	√	√
BARS Score	√	√	√	√
CGI-CB Score				√
SAS Score+	√	√	√	√
ADR recording	√	√	√	√
Concomitant medications	√	√	√	√

* Follow-up assessments were carried out by the physicians at the aforementioned approximate time intervals, as per the current standard medical practice for these subjects.

** Laboratory results were recorded, when available, including those that led to the decision for treatment switch.

*** Subjects were assessed using PANSS scale, in case that the reason for treatment switch is lack of efficacy of prior treatment.

+ SAS scale was only assessed in cases that the reason for treatment switch was extrapyramidal symptoms management.

7. TARGET PATIENT POPULATION, STUDY DISEASE AND SAMPLE SIZE

The target patient population for this study consisted of outpatients diagnosed with schizophrenia, who were treated at hospital outpatient clinics or private physicians' offices and had recently initiated a new antipsychotic treatment.

A total of 574 patients were enrolled into the study. Out of these patients, six violated the protocol procedures, making a total of 568 patients which were suitable for statistical analysis.

8. CRITERIA FOR EVALUATION (MAIN VARIABLES)

8.1 Primary endpoint – Primary variable

- CGI-CB scale score was recorded, and the percentage of subjects achieving a score of ≤ 4 at the end of the study was calculated.

8.2 Secondary endpoints

- Change in PANSS, CGI-S and CGI-I scales from baseline to the end of study treatment (Week 18) or the premature study withdrawal of the subject
- Change in SAS scale from baseline to the end of study
- Change in BARS scale from baseline to the end of study
- Change in body weight from baseline to the end of study
- Change in values of laboratory assessments from baseline to the end of study
- Change in severity of any other ADR

It shall be noted that each of the afore-mentioned secondary variables were assessed based on the prerequisite that they fell within the framework of normal clinical practice regarding the follow-up of the patient population. Depending on the reason for treatment switch, the respective variable was evaluated.

9. STATISTICAL METHODS

The analysis of data was based mainly on descriptive statistical methods. Continuous variables are presented by means of measures of central tendency and dispersion. Categorical variables are presented by frequency distribution tables. The relation between categorical variables is illustrated by contingency tables. The statistical significance of the changes, of the evaluation scales and laboratory measurements, from first to final visit, was assessed by means of a paired t–test. The 95% confidence intervals were calculated regarding the estimation of the primary endpoint.

Data control checks during Data Entry were performed according to the Data Management Plan.

All medical terminology was described according to MeDRA dictionary v13.1.

Data analysis was performed with the statistical software SPSS 17.0.

9.1 Population Analysis Sets:

9.1.1 Definition of the target population

The target population consisted of psychiatric outpatients diagnosed with schizophrenia which were treated at hospital outpatient clinics or private physicians' offices and had initiated a new antipsychotic treatment within two weeks before entry into the study. The sample population also met all inclusion criteria and had no exclusion criteria at enrollment.

A total number of 574 subjects were enrolled onto the study (Intention To Treat population (ITT)). No protocol violator was identified in the current trial. However, six patients violated the terms of the protocol, being either lost to follow-up or not having attended all scheduled visits and were excluded from the statistical analysis. The statistical analysis was performed on the Per Protocol Population (PPP; 568 subjects). The number of patients attending per visit can be seen in **Table 1**.

Table 1 Number of patients attending per visit

Visit Number	Number of patients attended
1st Visit	574
2nd Visit	571
3rd Visit	569
4th Visit	569 (one patient returned after missing visits 2 & 3)

9.2 Statistical Analysis Result

9.2.1 Descriptive Analysis:

Baseline patient characteristics and demographics are presented in **Table 2**. Upon enrollment to the study, the most common disorders found in the medical histories were psychiatric disorders (186 patients; 32.7%) and nervous system disorders (72 patients; 12.7%). An analytical listing of all disorders and their prevalence for the enrolled patients can be seen in **Table 3** and **Table 4**. Only 34.7% of patients were not receiving any concomitant medications during the study period. As seen in **Table 5**, from the patients which were taking concomitant medications during the study period (371 patients), the majority (247 patients) received only one concomitant medication.

Table 2 Demographic and baseline characteristics

Demographics		
Age (years)		
Mean ±SD	39.0±11.2	
Range	18–65	
Sex, *n* (%)		
Male	301	(53.0)
Female	267	(47.0)
BMI (kg/m^2)		
Mean ±SD	27.6 ± 4.7	
Range	17.7–50.8	
Educational level, *n (%)*		
Elementary	71	(12.5)
High school (Junior)	121	(21.3)
High school	217	(38.3)
Technical institution	90	(15.9)
University	68	(12.0)
Place of residence, *n (%)*		
Urban	397	(70.1)
Suburban	92	(16.3)
Rural	77	(13.6)
Living Conditions, *n (%)*		
Lives alone	86	(15.1)
Lives with wife	101	(17.8)
Lives with children, relatives /other	372	(65.5)
Nursing home, institution	8	(1.4)
Lives with wife & children	1	(0.2)
Employment, *n (%)*		
No	347	(61.2)
Yes	220	(38.8)
Time from diagnosis (year)		
Mean±SD	11.7 ± 12.3	
Range	0.5-41	

Table 3 Patient's medical history

Medical History (system organ class)	***n* (%)**
Psychiatric Disorders	186 (32.7)
Nervous System Disorders	72 (12.7)
Vascular Disorders	33 (5.8)
Metabolism & Nutrition Disorders	29 (5.1)
Endocrine Disorders	20 (3.5)
Respiratory, Thoracic & Mediastinal Disorders	6 (1.1)
Gastrointestinal Disorders	4 (0.7)
Musculoskeletal & Connective Tissue Disorders	3 (0.5)
Reproductive System & Breast Disorders	2 (0.4)
Respiratory, Thoracic & Mediastinal Disorders	2 (0.4)
Skin & Subcutaneous Tissue Disorders	2 (0.4)
Blood & Lymphatic System Disorders	1 (0.2)
General Disorders And Administration Site Conditions	1 (0.2)
Hepatobiliary Disorders	1 (0.2)
Peripheral Neuropathies	1 (0.2)

Table 4 Patient's medical history (Medra Terms)

Medical History	(n%)
Psychiatric Disorders (n=186)	
Stress	68 (36.6)
Depression	39 (21.0)
Insomnia	30 (16.1)
Psychotic Disorder	11 (5.9)
Anxiety	10 (5.4)
Agitation	6 (3.2)
Impulsive Behaviour	6 (3.2)
Psychomotor Hyperactivity	3 (1.6)
Sleep Disorder	3 (1.6)
Obsessive–Compulsive Disorder	2 (1.1)
Panic Disorder	2 (1.1)
Akathisia	1 (0.5)
Drug Abuse	1 (0.5)
Dyssomnia	1 (0.5)
Feeling Guilty	1 (0.5)
Panic Attack	1 (0.5)
Social Avoidant Behaviour	1 (0.5)
Nervous System Disorders (n=72)	
Extrapyramidal Disorder	65 (90.3)
Epilepsy	2 (2.8)
Migraine	1 (1.4)
Parkinsonism	1 (1.4)
Seizures	1 (1.4)
Tardive Dyskinesia	1 (1.4)
Tremor	1 (1.4)
Vascular Disorders (n=33)	
Hypertension	29 (87.9)
Aortic Aneurysm	1 (3.0)
Haemangioma (Facial)	1 (3.0)

Table 4 Patient's medical history (Medra Terms)

Medical History	(n%)
Psychiatric Disorders (n=186)	
Stress	68 (36.6)
Hypotension Orthostatic	1 (3.0)
Orthostatic Hypertension	1 (3.0)
Metabolism & Nutrition Disorders (n=29)	
Diabetes Mellitus	15 (51.7)
Hyperlipidaemia	7 (24.1)
Hypercholesterolaemia	2 (6.9)
Obesity	2 (6.9)
Dyslipidaemia	1 (3.4)
Iron Defficiency Anaemia	1 (3.4)
T1 Diabetes Mellitus	1 (3.4)
Endocrine Disorders (n=20)	
Hypothyroidism	10 (50.0)
Thyroid Disorder	6 (30.0)
Hyperprolactinaemia	3 (15.0)
Thyroid Gland Abscess	1 (5.0)

Table 5 Number of concomitant medications received during the study period*

No. of concomitant medications	n (%)
1	247 (43.5)
2	95 (16.7)
3	20 (3.5)
4	7 (1.2)
5	1 (0.2)
6	1 (0.2)
Total	371 (65.3)

*371/568 (65.3%) patients were receiving at least one concomitant medication

9.2.2 Primary Objective:

Evaluation of the outcome of treatment switch, defined as an improvement in CGI-CB scale (Clinical Global Impression – Clinical Benefit).

During the study, CGI-CB scores were recorded for all patients. Subjects achieving a CGI-CB score of ≤ 4 at the end of the study were considered as having clinically benefited from the change of antipsychotic therapy. The percentage of patients with a CGI–CB of ≤ 4 at the final visit was 87.9% [95%CI: (84.9–90.4)] (**Table 6**). The previous antipsychotic treatments of the patients with CGI–CB≤ 4 at the final visit and the reasons for change in medication can be seen in **Table 7** and **Table 8**.

Table 6 Percentage of patients with CGI–CB ≤ 4 at the final visit

Value of CGI-CB	***n* (%)**
CGI–CB > 4	69 (12.1)
CGI–CB ≤ 4	499 (87.9)
Total	568

Table 7 Frequency and percentage of patients with CGI–CB ≤ 4, by reason for change from previous antipsychotic therapy.

Current antipsychotic treatment	**Lack of Efficacy (Only)** ***n(%)***	**Lack of Safety (Only)** ***n(%)***	**Lack of Efficacy & Safety** ***n(%)***
Amisulpride	15 (100.0)	4 (80.0)	2 (66.7)
Aripiprazole	13 (81.3)	31 (83.8)	2 (66.7)
Ziprasidone	5 (83.3)	15 (93.8)	4 (100.0)
Clozapine	9 (100.0)	1 (50.0)	2 (100.0)
Quetiapine & Quetiapine XR	89 (87.3)	174 (90.2)	17 (73.9)
Olanzapine	9 (81.8)	27 (96.4)	8 (100.0)
Paliperidone	11 (91.7)	17 (89.5)	4 (100.0)
Risperidone	16 (80.0)	10 (83.3)	2 (100.0)
Other Antipsychotic	6 (75.0)	5 (71.4)	1 (100.0)
Total	**173 (86.9)**	**284 (89.0)**	**42 (84.0)**

Table 8 **Frequency and percentage of patients with CGI–CB≤4, per aspect of safety per reason for change from previous antipsychotic therapy.**

Current antipsychotic treatment	Lack of Efficacy (N=369) *n(%)*	Lack of Safety (N =249) *n(%)*	Extrapyramidal Symptoms (N =111) *n(%)*	Weight Gain (N =149) *n(%)*	Hyperlipidaemia or/and Glucose increase (N =24) *n(%)*	Hyperprolactinaemia (N =39) *n(%)*	Lack of Tolerance (N =42) *n(%)*	Other Reason (N =49) *n(%)*
Amisulpride	17 (94.4)	6 (75.0)	1 (100.0)	2 (50.0)	3 (100.0)	5 (100.0)	2 (66.7)	2 (66.7)
Aripiprazole	15 (78.9)	33 (82.5)	4 (80.0)	21 (80.8)	0 (0.0)	0 (0.0)	2 (100.0)	3 (60.0)
Ziprasidone	9 (90.0)	19 (95.0)	4 (100.0)	10 (90.9)	3 (100.0)	0 (0.0)	3 (100.0)	3 (100.0)
Clozapine	11 (100.0)	3 (75.0)	2 (100.0)	1 (100.0)	0 (0.0)	1 (50.0)	0 (0.0)	0 (0.0)
Quetiapine & Quet. XR	106 (84.8)	191(88.4)	59 (85.5)	83 (95.4)	12 (92.3)	19 (86.4)	14 (66.7)	21 (77.8)
Olanzapine	17 (89.5)	35 (97.2)	19 (100.0)	1 (100.0)	1 (100.0)	6 (85.7)	3 (100.0)	5 (83.3)
Paliperidone	15 (93.8)	21 (91.3)	7 (87.5)	8 (100.0)	1 (100.0)	2 (100.0)	4 (100.0)	4 (80.0)
Risperidone	18 (81.8)	12 (85.7)	3 (100.0)	5 (71.4)	0 (0.0)	0 (0.0)	3 (100.0)	1 (100.0)
Other Antipsychotic	7 (77.8)	6 (75.0)	0 (0.0)	2 (50.0)	0 (0.0)	1 (100.0)	3 (100.0)	0 (0.0)
Total	**215 (86.3)**	**326(88.3)**	**99 (89.2)**	**133 (89.3)**	**20 (83.3)**	**34 (87.2)**	**34 (81.0)**	**39 (78.0)**

9.2.3 Secondary Objectives:

To document the reasons leading physicians to the switch in antipsychotic treatment

The reasons for physicians switching antipsychotic treatments can be seen in **Table 9**. The most frequent reason for a change in antipsychotic therapy was due to a lack of safety (369 patients; 65.0%). From the patients which changed due to lack of safety, the main reasons for the treatment change were weight gain (40.4%) or extrapyramidal symptoms (30.1%).

A detailed list of the reasons of change from previous antipsychotic treatment for each therapeutic agent can be seen in **Table 10**.

Table 11 and **Table 12** show the reasons for change of all antipsychotic treatments which were classified as typical adverse events or "other" adverse events.

Table 9 Reason for change from previous antipsychotic treatment

Reason for change from the previous antipsychotic treatment	***n=568*** ***n (%)***
Lack of Safety (Only)	319 (56.2)
Lack of Efficacy (Only)	199 (35.0)
Lack of Efficacy & Safety	50 (8.8)
Analytically, *n (%)*	***n=568***
Lack of Safety (Total)	369 (65.0)
Lack of Efficacy (Total)	249 (43.8)
Lack of Safety (Analytically), *n (%)*	***n=369***
Weight gain	149 (40.4)
Extrapyramidal Symptoms	111 (30.1)
Lack of Tolerance	42 (11.4)
Hyperprolactinaemia	39 (10.6)
Hyperlipidaemia and/or Glucose increase	24 (6.5)
Other reason	49 (13.3)
Stress-Insomnia-Anxiety-Akathisia	16 (32.7)
Sleepiness-Drowsiness	12 (24.5)
Gynecological Dysfunctions	6 (12.2)
Sexual Disorders	6 (12.2)
Other Adverse Events	10 (20.4)

Table 10 Previous antipsychotic treatment and reason for its change

Previous Antipsychotic Treatment, *n (%)*	Lack of Efficacy	Lack of Safety	Lack of Efficacy & Safety	**Total**
Amisulpride	15 (30.6)	35 (71.4)	1 (2.0)	49
Aripiprazole	55 (75.3)	25 (34.2)	7 (9.6)	73
Ziprasidone	32 (84.2)	8 (21.1)	2 (5.3)	38
Clozapine	0 (0.0)	1 (100.0)	0 (0.0)	1
Quetiapine & Quet XR	11 (64.7)	7 (41.2)	1 (5.9)	17
Olanzapine	41 (25.3)	138 (85.2)	17 (10.5)	162
Paliperidone	8 (57.1)	8 (57.1)	2 (14.3)	14
Risperidone	53 (39.8)	91 (68.4)	11 (8.3)	133
Other Antipsychotic	34 (42.0)	56 (69.1)	9 (11.1)	81
Total	249 (43.8)	369 (65.0)	50 (8.8)	568

Table 11 Previous antipsychotic treatment and reason for its change (Patients that changed treatment due to AE)

Previous Antipsychotic Treatment	Extrapyramidal Symptoms n (%)	Weight Gain n (%)	Hyperlipidaemia and/or Glucose increase n (%)	Hyperprolactinaemia n (%)	Lack of Tolerance n (%)	Other AE n (%)	**Total**
Amisulpride	10 (28.6)	3 (8.6)	0 (0.0)	17 (48.6)	4 (11.4)	5 (14.3)	35
Aripiprazole	4 (16.0)	3 (12.0)	2 (8.0)	0 (0.0)	13 (52.0)	10 (40.0)	25
Ziprasidone	1 (12.5)	3 (37.5)	0 (0.0)	0 (0.0)	3 (37.5)	1 (12.5)	8
Clozapine	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	0 (0.0)	1
Quetiapine & Quet XR	0 (0.0)	2 (28.6)	0 (0.0)	0 (0.0)	4 (57.1)	2 (28.6)	7
Olanzapine	3 (2.2)	116(84.1)	21 (15.2)	2 (1.4)	4 (2.9)	6 (4.3)	138
Paliperidone	3 (37.5)	3 (37.5)	0 (0.0)	2 (25.0)	0 (0.0)	2 (25.0)	8
Risperidone	46 (50.5)	17 (18.7)	1 (1.1)	17 (18.7)	8 (8.8)	16 (17.6)	91
Other Antipsychotic	44 (78.6)	2 (3.6)	0 (0.0)	1 (1.8)	5 (8.9)	7 (12.5)	56
Total	111 (30.1)	149 (40.4)	24 (6.5)	39 (10.6)	42 (11.4)	49 (13.3)	369

Table 12 Previous antipsychotic treatment and reason for change (when changed due to "other AE")

Previous Antipsychotic Treatment	Sleepiness-Drowsiness n (%)	Stress-Insomnia-Anxiety-Akathisia n (%)	Gynecological Dysfunctions n (%)	Sexual Disorders n (%)	Other AE n (%)	**Total**
Amisulpride	0 (0.0)	2 (40.0)	2 (40.0)	0 (0.0)	1 (20.0)	5
Aripiprazole	0 (0.0)	8 (80.0)	0 (0.0)	0 (0.0)	2 (20.0)	10
Ziprasidone	0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	1
Quetiapine & Quet XR	1 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (50.0)	2
Olanzapine	4 (66.7)	2 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	6
Paliperidone	0 (0.0)	0 (0.0)	1 (50.0)	0 (0.0)	1 (50.0)	2
Risperidone	4 (25.0)	3 (18.8)	2 (12.5)	5 (31.3)	3 (18.8)	16
Other Antipsychotic	3 (42.9)	0 (0.0)	1 (14.3)	1 (14.3)	2 (28.6)	7
Total	12 (24.5)	16 (32.7)	6 (12.2)	6 (12.2)	10 (20.4)	49

Documentation of treatment options

The relation between the reasons of change of previous antipsychotic treatment and the type of previous antipsychotic treatments can be seen in **Tables 13-15**.

The relation between the reasons of change of the previous antipsychotic treatment and the type of current antipsychotic treatment can be seen in **Tables 16-18**.

Table 13 **Relation between reason of change of previous antipsychotic treatment and the type of previous antipsychotic treatment**

		Previous Antipsychotic Treatment									
Reason of Change		**AMISULPRIDE**	**ARIPIPRAZOLE**	**ZIPRASIDONE**	**CLOZAPINE**	**QUETIAPINE & QUETIAPINE XR**	**OLANZAPINE**	**PALIPERIDONE**	**RISPERIDONE**	**OTHER ANTIPSYCHOTIC**	**TOTAL**
Lack of Efficacy	***n***	15	55	32	0	11	41	8	53	34	249
	(%)	(6.0)	(22.1)	(12.9)	(0.0)	(4.4)	(16.5)	(3.2)	(21.3)	(13.7)	
Lack of Safety	***n***	35	25	8	1	7	138	8	91	56	369
	(%)	(9.5)	(6.8)	(2.2)	(0.3)	(1.9)	(37.4)	(2.2)	(24.7)	(15.2)	
Lack of Efficacy & Safety	***n***	1	7	2	0	1	17	2	11	9	50
	(%)	(2.0)	(14.0)	(4.0)	(0.0)	(2.0)	(34.0)	(4.0)	(22.0)	(18.0)	

Table 14 **Relation between reason of change of previous antipsychotic treatment and the type of previous antipsychotic treatment (patients that changed treatment due to AE)**

		Previous Antipsychotic Treatment									
Type of AE:		**AMISULPRIDE**	**ARIPIPRAZOLE**	**ZIPRASIDONE**	**CLOZAPINE**	**QUETIAPINE & QUETIAPINE XR**	**OLANZAPINE**	**PALIPERIDONE**	**RISPERIDONE**	**OTHER ANTIPSYCHOTIC**	**TOTAL**
Extrapyramidal Symptoms	***n***	10	4	1	0	0	3	3	46	44	111
	(%)	(9.0)	(3.6)	(0.9)	(0.0)	(0.0)	(2.7)	(2.7)	(41.4)	(39.6)	
Weight Gain	***n***	3	3	3	0	2	116	3	17	2	149
	(%)	(2.0)	(2.0)	(2.0)	(0.0)	(1.3)	(77.9)	(2.0)	(11.4)	(1.3)	
Hyperlipidaemia and/or Glucose increase	***n***	0	2	0	0	0	21	0	1	0	24
	(%)	(0.0)	(8.3)	(0.0)	(0.0)	(0.0)	(87.5)	(0.0)	(4.2)	(0.0)	
Hyper-prolactinaemias	***n***	17	0	0	0	0	2	2	17	1	39
	(%)	(43.6)	(0.0)	(0.0)	(0.0)	(0.0)	(5.1)	(5.1)	(43.6)	(2.6)	
Lack of Tolerance	***n***	4	13	3	1	4	4	0	8	5	42
	(%)	(9.5)	(31.0)	(7.1)	(2.4)	(9.5)	(9.5)	(0.0)	(19.0)	(11.9)	
Other AE	***n***	5	10	1	0	2	6	2	16	7	49
	(%)	(10.2)	(20.4)	(2.0)	(0.0)	(4.1)	(12.2)	(4.1)	(32.7)	(14.3)	

Table 15 **Relation between reason of change of previous antipsychotic treatment and the type of previous antipsychotic treatment (patients that changed treatment due to "other AE")**

		Previous Antipsychotic Treatment									
Change due to:		**AMISULPRIDE**	**ARIPIPRAZOLE**	**ZIPRASIDONE**	**CLOZAPINE**	**QUETIAPINE & QUETIAPINE XR**	**OLANZAPINE**	**PALIPERIDONE**	**RISPERIDONE**	**OTHER ANTI-PSYCHOTIC**	**TOTAL**
Sleepiness-drowsiness	***n***	0	0	0	0	1	4	0	4	3	12
	(%)	(0.0)	(0.0)	(0.0)	(0.0)	(8.3)	(33.3)	(0.0)	(33.3)	(25.0)	
Stress-Insomnia-Anxiety-Akathisia	***n***	2	8	1	0	2	0	3	0	0	16
	(%)	(12.5)	(50.0)	(6.3)	(0.0)	(12.5)	(0.0)	(18.8)	(0.0)	(0.0)	
Gynecological Dysfunctions	***n***	2	0	0	0	0	0	1	2	1	6
	(%)	(33.3)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(16.7)	(33.3)	(16.7)	
Sexual Disorders	***n***	0	0	0	0	0	0	0	5	1	6
	(%)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(83.3)	(16.7)	
Other AE	***n***	1	2	0	0	1	0	1	3	2	10
	(%)	(10.0)	(20.0)	(0.0)	(0.0)	10.0)	(0.0)	(10.0)	(30.0)	(20.0)	

Table 16 Relation between reason of change of previous antipsychotic treatment and the type of current antipsychotic treatment

		Current Antipsychotic Treatment									
Change due to:		**AMISULPRIDE**	**ARIPIPRAZOLE**	**ZIPRASIDONE**	**CLOZAPINE**	**QUETIAPINE & QUETIAPINE XR**	**OLANZAPINE**	**PALIPERIDONE**	**RISPERIDONE**	**OTHER ANTIPSYCHOTIC**	**TOTAL**
Lack of Efficacy	***n***	18	19	10	11	125	19	16	22	9	249
	(%)	7.2	7.6	4.0	4.4	50.2	7.6	6.4	8.8	3.6	
Lack of Safety	***n***	8	40	20	4	216	36	23	14	8	369
	(%)	2.2	10.8	5.4	1.1	58.5	9.8	6.2	3.8	2.2	
Lack of Efficacy & Lack of Safety	***n***	3	3	4	2	23	8	4	2	1	50
	(%)	6.0	6.0	8.0	4.0	46.0	16.0	8.0	4.0	2.0	

Table 17 **Relation between reason of change of previous antipsychotic treatment and the type of current antipsychotic treatment (patients that changed treatment due to AE)**

		Current Antipsychotic Treatment									
Type of AE:		**AMISULPRIDE**	**ARIPIPRAZOLE**	**ZIPRASIDONE**	**CLOZAPINE**	**QUETIAPINE & QUETIAPINE XR**	**OLANZAPINE**	**PALIPERIDONE**	**RISPERIDONE**	**OTHER ANTIPSYCHOTIC**	**TOTAL**
Extrapyramidal Symptoms	***n***	1	5	4	2	69	19	8	3	0	111
	(%)	0.9	4.5	3.6	1.8	62.2	17.1	7.2	2.7	0.0	
Weight Gain	***n***	4	26	11	1	87	1	8	7	4	149
	(%)	2.7	17.4	7.4	0.7	58.4	0.7	5.4	4.7	2.7	
Hyperlipidaemia and/or Glucose increase	***n***	0	3	3	0	13	1	1	1	2	24
	(%)	0.0	12.5	12.5	0.0	54.2	4.2	4.2	4.2	8.3	
Hyperprolactinaemiaς	***n***	0	5	0	2	22	7	2	0	1	39
	(%)	0.0	12.8	0.0	5.1	56.4	17.9	5.1	0.0	2.6	
Lack of Tolerance	***n***	3	2	3	0	21	3	4	3	3	42
	(%)	7.1	4.8	7.1	0.0	50.0	7.1	9.5	7.1	7.1	
Other AE	***n***	2	5	3	0	27	6	5	1	0	49
	(%)	4.1	10.2	6.1	0.0	55.1	12.2	10.2	2.0	0.0	

Table 18 **Relation between reason of change of previous antipsychotic treatment and the type of current antipsychotic treatment (patients that changed treatment due to "other AE")**

		Current Antipsychotic Treatment									
Type of "Other AE":		**AMISULPRIDE**	**ARIPIPRAZOLE**	**ZIPRASIDONE**	**CLOZAPINE**	**QUETIAPINE & QUETIAPINE XR**	**OLANZAPINE**	**PALIPERIDONE**	**RISPERIDONE**	**OTHER ANTIPSYCHOTIC**	**TOTAL**
Sleepiness-drowsiness	***n***	1	3	1	0	3	2	2	0	0	12
	(%)	8.3	25.0	8.3	0.0	25.0	16.7	16.7	0.0	0.0	
Stress-Insomnia-Anxiety-Akathisia	***n***	0	0	0	0	14	2	0	0	0	16
	(%)	0.0	0.0	0.0	0.0	87.5	12.5	0.0	0.0	0.0	
Gynecological Dysfunctions	***n***	0	1	0	0	2	1	2	0	0	6
	(%)	0.0	16.7	0.0	0.0	33.3	16.7	33.3	0.0	0.0	
Sexual Disorders	***n***	0	1	1	0	4	0	0	0	0	6
	(%)	0.0	16.7	16.7	0.0	66.7	0.0	0.0	0.0	0.0	
Other AE	***n***	1	0	1	0	4	2	1	1	0	10
	(%)	10.0	0.0	10.0	0.0	40.0	20.0	10.0	10.0	0.0	

Efficacy assessments

In addition to the changes in CGI-CB scores, the observed changes in PANSS, CGI-S and CGI-I scales from baseline to the end of study treatment were also used as efficacy assessments. The mean of all the end of study efficacy scales decreased for all current antipsychotic therapies, indicating a statistically significant increase in efficacy after the therapy switch (**Table 20**). The mean change in CGI-S scores for all medications was -1.14 95% CI [-1.22, -1.05], p<0.001, CGI-I score -0.7095% CI [-0.76, -0.64], p<0.001 and PANSS was -31.69 95% CI [-34.42, -28.96], p<0.001, at the end of study.

Table 19 Levels of each index/measure at each visit

	Index/measure	Visit 1 Mean ± SD (n)	Visit 2 Mean ± SD (n)	Visit 3 Mean ± SD (n)	Visit 4 Mean ± SD (n)
	CGI–S	4.1 ± 1.1 (568)	–	–	3.0 ± 1.1 (568)
	CGI–I	–	2.9 ± 0.8 (568)	2.5 ± 1.6 (566)	2.2 ± 0.8 (568)
	BARS %	86.1 ± 18.2 (568)	93.3 ± 10.7 (568)	95.4 ± 8.7 (567)	95.8 ± 8.5 (568)
Reason for previous treatment change					
Lack of Efficacy	PANSS	92.9 ± 28.2 (249)	77.4 ± 26.3 (249)	67.2 ± 23.4 (249)	61.2 ± 22.7 (249)
Extrapyramidal symptoms	SAS	14.5 ± 9.6 (111)	7.1 ± 9.3 (111)	3.4 ± 8.9 (111)	3.1 ± 11.3 (111)
Weight Gain	Weight (kg)	89.6 ± 17.3 (149)	87.6 ± 16.5 (149)	84.6 ± 16.3 (149)	82.8 ± 16.0 (149)
Glucose increase	Glucose (mmol/L)	48.3 ± 69.4 (18)	42.1 ± 63.2 (14)	41.4 ± 56.6 (13)	36.2 ± 49.8 (18)
Hyperpro-lactinaemia	Hyper-plactinaemia	83.6 ±48.7 (39)	54.0 ± 37.7 (29)	34.6 ± 24.8 (30)	21.3 ± 10.8 (39)
Hyperlipidaemia	Total Cholesterol (mmol/L)	81.7 ± 108.0 (11)	97.5 ± 116.6 (8)	87.0 ± 109.2 (9)	72.0 ± 96.2 (11)
	LDL Cholesterol (mmol/L)	75.8 ± 92.2 (8)	89.2 ± 93.2 (6)	89.9 ± 93.0 (6)	70.2 ± 84.4 (8)
	HDL Cholesterol (mmol/L)	37.4 ± 17.9 (10)	37.5 ± 18.3 (7)	37.7 ± 17.7 (7)	41.6 ± 17.7 (10)
	Triglicerides (mmol/L)	124.0 ± 178.8 (10)	141.3 ±161.7 (8)	110.3 ± 134.2 (9)	92.4 ± 112.3 (10)

Table 20 Estimation of the mean change of each index/measurement during the trial

Scale / measurement	N	Mean Change V4-V1	Lower 95% CI	Upper 95% CI	p–value
BARs	568	9.73	8.38	11.08	<0.0001
CGIs	568	–1.14	–1.22	–1.05	<0.0001
CGIi	568	–0.70	–0.76	–0.64	<0.0001
PANSS	249	–31.69	–34.42	–28.96	<0.0001
SAS	111	–11.30	–13.09	–9.51	<0.0001
Weight (kg)	149	–6.85	–7.75	–5.96	<0.0001
Hypeprolactinaemia (ng/ml)	39	–62.30	–76.70	–47.90	<0.0001
Total Cholesterol (mmol/L)	11	–9.73	–19.32	–0.14	0.047
LDL(mmol/L)	8	–5.52	–21.65	10.61	0.445
HDL(mmol/L)	10	4.20	–4.10	12.50	0.282
Triglycerides (mmol/L)	10	–31.58	–84.77	21.61	0.212
Glucose (mmol/L)	17	–12.08	–22.23	–1.93	0.022

Table 21 PANSS scores at each study visit

	PANSS, *Mean* ± *SD*			
Current antipsychotic therapy (n=249)	**Visit 1**	**Visit 2**	**Visit 3**	**Visit 4**
Amisulpride (n=18)	87.6 ± 18.1	65.3 ± 14.4	54.8 ± 15.2	50.9 ±14.7
Aripiprazole (n=19)	90.6 ± 32.0	78.9 ±30.9	68.0 ± 27.6	66.4 ± 27.1
Ziprasidone (n=10)	83.8 ± 16.5	70.2 ± 19.2	62.8 ± 16.1	58.4 ± 17.9
Clozapine (n=11)	103.0 ± 30.5	79.9 ± 28.8	63.8 ± 26.6	50.9 ± 15.8
Quetiapine & Quetiapine XR (n=125)	94.3 ± 30.2	80.9 ± 27.5	71.4 ± 25.0	64.8 ± 25.2
Olanzapine (n=19)	95.2 ± 27.1	74.9 ± 27.4	63.3 ± 18.2	54.2 ± 15.0
Paliperidone (n=16)	87.6 ± 27.4	68.0 ± 22.2	59.4 ± 18.7	53.9 ± 15.5
Risperidone (n=22)	91.0 ± 25.5	74.0 ± 24.7	63.6 ± 19.7	60.3 ± 18.0
Other Antipsychotic (n=9)	95.2 ± 28.7	84.3 ± 25.9	72.2 ± 23.5	65.7 ± 25.4

Table 22 Mean change (and 95%CI) of PANSS from first to final study visit

Scale / measurement	Current therapy	N	Mean Change	Lower 95% CI	Upper 95% CI	p–value
PANSS	Amisulpride	18	–36.67	–46.18	–27.16	<0.0001
	Aripiprazole	19	–24.21	–36.12	–12.31	<0.0001
	Ziprasidone	10	–25.40	–34.42	–16.38	<0.0001
	Clozapine	11	–52.09	–67.20	–36.99	<0.0001
	Quetiapine & Quetiapine XR	125	–29.50	–33.27	–25.72	<0.0001
	Olanzapine	19	–40.95	–54.95	–26.95	<0.0001
	Paliperidone	16	–33.63	–44.91	–22.34	<0.0001
	Risperidone	22	–30.68	–37.30	–24.06	<0.0001
	Other Antipsychotic	9	–29.56	–44.06	–15.05	0.002

Table 23 Patients' CGI-S and CGI-I scores at each study visit

Current antipsychotic therapy, (n=568)	CGI–S, *Mean* ± *SD*		CGI–I, *Mean* ± *SD*		
	Visit 1	Visit 4	Visit 2	Visit 3	Visit 4
Amisulpride (n=23)	4.3 ± 1.0	2.7 ± 1.2	2.5 ± 0.8	2.3 ± 1.1	2.0 ± 0.9
Aripiprazole (n=56)	4.0 ± 0.9	2.9 ± 1.0	3.0 ± 0.9	2.7 ± 1.0	2.3 ± 0.8
Ziprasidone (n=26)	3.7 ± 1.2	3.0 ± 0.9	3.0 ± 0.8	2.8 ± 0.7	2.6 ± 0.8
Clozapine (n=13)	5.1 ± 0.8	2.7 ± 1.0	2.5 ± 0.8	2.0 ± 0.7	1.5 ± 0.5
Quetiapine & Quetiapine XR (n=318)	4.1 ± 1.1	3.0 ± 1.1	3.0 ± 0.8	2.5 ± 0.9	2.2 ± 0.8
Olanzapine (n=47)	3.9 ± 1.0	2.7 ± 0.9	2.6 ± 0.7	2.2 ± 0.7	2.0 ± 0.7
Paliperidone (n=35)	4.1 ± 0.9	2.8 ± 0.9	2.8 ± 0.8	2.5 ± 0.9	2.2 ± 0.9
Risperidone (n=34)	4.3 ± 0.9	3.3 ± 1.0	2.6 ± 0.8	2.3 ± 0.8	2.1 ± 0.6
Other Antipsychotic (n=16)	4.6 ± 1.5	3.2 ± 1.2	3.3 ± 0.6	2.9 ± 0.9	2.4 ± 0.9

Table 24: Mean change (and 95%CI) of CGIi and CGIs from first to final study visit.

Scale / measurement	Current therapy	N	Mean Change	Lower 95% CI	Upper 95% CI	p–value
CGIi *	Amisulpride	23	–0.43	–0.65	–0.22	<0.0001
	Aripiprazole	56	–0.71	–0.90	–0.53	<0.0001
	Ziprasidone	26	–0.38	–0.71	–0.06	0.022
	Clozapine	13	–1.08	–1.60	–0.56	0.001
	Quetiapine & Quetiapine XR	318	–0.76	–0.85	–0.67	<0.0001
	Olanzapine	47	–0.64	–0.82	–0.46	<0.0001
	Paliperidone	35	–0.57	–0.83	–0.32	<0.0001
	Risperidone	34	–0.50	–0.76	–0.24	<0.0001
	Other Antipsychotic	16	–0.88	–1.20	–0.55	<0.0001
CGIs	Amisulpride	23	–1.57	–2.17	–0.96	<0.0001
	Aripiprazole	56	–1.05	–1.31	–0.80	<0.0001
	Ziprasidone	26	–0.73	–1.04	–0.42	<0.0001
	Clozapine	13	–2.38	–2.97	–1.80	<0.0001
	Quetiapine & Quetiapine XR	318	–1.08	–1.19	–0.97	<0.0001
	Olanzapine	47	–1.23	–1.54	–0.93	<0.0001
	Paliperidone	35	–1.23	–1.58	–0.87	<0.0001
	Risperidone	34	–1.03	–1.39	–0.67	<0.0001
	Other Antipsychotic	16	–1.38	–1.89	–0.86	<0.0001

* visit 2 – visit 4

Change in extrapyramidal symptoms

The change in extrapyramidal symptoms was evaluated according to the change in SAS scores from baseline to the end of study.

Table 25 SAS scores at each study visit

	SAS			
Current antipsychotic therapy, (n=111)	**Visit 1** *Mean ± SD*	**Visit 2** *Mean ± SD*	**Visit 3** *Mean ± SD*	**Visit 4** *Mean ± SD*
Amisulpride (n=1)	13.0	11.0	6.0	9.0
Aripiprazole (n=5)	10.4 ± 4.3	3.8 ± 3.3	2.0 ± 1.6	0.8 ± 1.3
Ziprasidone (n=4)	7.3 ± 3.1	3.5 ± 4.0	2.8 ± 3.6	2.0 ± 2.7
Clozapine (n=2)	13.0 ± 0.0	11.0 ± 2.8	3.5 ± 4.9	3.5 ± 4.9
Quetiapine & Quetiapine XR (n=68)	15.2 ± 6.7	6.8 ± 5.1	2.6 ± 3.7	1.7 ± 2.8
Olanzapine (n=19)	11.7 ± 5.1	5.3 ± 4.8	1.6 ± 1.8	0.8 ± 1.5
Paliperidone (n=9)	19.9 ± 27.0	14.4 ± 28.4	12.3 ± 29.0	11.5 ± 28.6
Risperidone (n=3)	15.7 ± 3.1	11.7 ± 2.5	7.3 ± 2.5	28.3 ± 44.7
Other Antipsychotic (n=0)	–	–	–	–

Table 26 Mean change (and 95%CI) of SAS from first to final study visit

Scale / measurement	**Current therapy**	**N**	**Mean Change V4-V1**	**Lower 95% CI**	**Upper 95% CI**	**p–value**
SAS	Aripiprazole	5	–9.60	–16.21	–2.99	0.016
	Ziprasidone	4	–5.25	–8.78	–1.72	0.018
	Clozapine	2	–9.50	–53.97	34.97	NA
	Quetiapine & Quetiapine XR	68	–13.50	–15.23	–11.77	<0.0001
	Olanzapine	19	–10.89	–13.42	–8.37	<0.0001
	Paliperidone	9	–8.39	–10.33	–6.45	<0.0001
	Risperidone	3	12.67	–91.32	116.65	NA

Weight change

The change in body weight from baseline to the end of study was evaluated for the 149 patients whose reason for therapy change was due to weight gain.

Table 27 Patients' weight levels at each study visit

	Weight (kg)			
	Visit 1	**Visit 2**	**Visit 3**	**Visit 4**
Current antipsychotic therapy, (n=149)	*Mean ± SD*	*Mean ± SD*	*Mean ± SD*	*Mean ± SD*
Amisulpride (n=4)	89.3 ± 8.8	88.3 ± 9.0	86.8 ± 8.7	85.4 ± 8.4
Aripiprazole (n=26)	89.3 ± 19.5	87.7 ± 19.2	84.8 ± 19.2	82.3 ± 18.8
Ziprasidone (n=11)	95.2 ± 19.2	92.6 ± 18.1	89.4 ± 16.8	88.0 ± 17.8
Clozapine (n=1)	87.0	82.5	79.0	78.3
Quetiapine & Quetiapine XR (n=88)	89.3 ± 17.5	87.3 ± 16.5	84.1 ± 16.2	82.5 ± 15.7
Olanzapine (n=1)	90.0	88.0	85.0	83.0
Paliperidone (n=7)	92.5 ± 13.4	90.9 ± 12.5	88.3 ± 13.2	85.4 ± 14.2
Risperidone (n=7)	85.8 ± 20.9	82.7 ± 19.5	81.5 ± 20.3	79.6 ± 18.9
Other Antipsychotic (n=4)	86.0 ± 7.8	83.5 ± 6.6	79.8 ± 7.7	78.0 ± 8.2

Table 28 Mean change (and 95%CI) of weight from first to final study visit

Scale / measurement	**Current therapy**	**N**	**Mean Change V4-V1**	**Lower 95% CI**	**Upper 95% CI**	**p–value**
Weight (kg)	Amisulpride	4	–3.88	–5.23	–2.52	0.003
	Aripiprazole	26	–7.03	–8.39	–5.66	<0.0001
	Ziprasidone	11	–7.14	–8.88	–5.40	<0.0001
	Quetiapine & Quetiapine XR	88	–6.85	–8.29	–5.42	<0.0001
	Paliperidone	7	–7.14	–10.29	–4.00	0.001
	Risperidone	7	–6.20	–8.27	–4.13	<0.0001
	Other Antipsychotic	4	–8.00	–13.03	–2.97	0.015

Change in values of laboratory assessments from baseline to the end of study

Out of the 18 patients who switched therapy due to high glucose levels, after medication switch, the mean glucose levels were reduced at the end of the study, but could not be

evaluated (**Table 30**).

Table 29 Patients' glucose levels at each study visit*

Current antipsychotic therapy, (n=18)	Glucose (mmol/L)			
	Visit 1 *Mean ± SD*	**Visit 2** *Mean ± SD*	**Visit 3** *Mean ± SD*	**Visit 4** *Mean ± SD*
Amisulpride (n=0)	–	–	–	–
Aripiprazole (n=2)	116.9 ± 145.8	106.5 ± 132.2	85.5 ± 105.4	80.3 ± 98.6
Ziprasidone (n=2)	71.0 ± 97.7	59.7 ± 82.4	56.8 ± 78.0	55.7 ± 76.9
Clozapine (n=0)	–	–	–	–
Quetiapine & Quetiapine XR (n=10)	44.9 ± 62.3	30.1 ± 46.4	34.5 ± 48.4	34.4 ± 45.6
Olanzapine (n=0)	–	–	–	–
Paliperidone (n=1)	15.5	14.0	11.0	11.0
Risperidone (n=1)	12.2	–	–	11.3
Other Antipsychotic (n=2)	8.7 ± 10.4	1.1	1.1	6.8 ± 8.3

Table 30 Mean change (and 95%CI) of Glucose from first to final study visit

Scale / measurement	Current therapy	N	Mean Change V4-V1	Lower 95% CI	Upper 95% CI	p–value
Glucose (mmol/L)	Aripiprazole	2	–36.7	–460.4	387.1	NA
	Ziprasidone	2	–15.3	–202.1	171.5	NA
	Quetiapine & Quetiapine XR	10	–10.4	–23.0	2.1	0.093
	Other Antipsychotic	2	–1.9	–20.2	16.5	NA

Table 31 Patients' cholesterol levels at each study visit*

Current antipsychotic therapy, (n=11)	Total Cholesterol (mmol/L)			
	Visit 1 *Mean ± SD*	**Visit 2** *Mean ± SD*	**Visit 3** *Mean ± SD*	**Visit 4** *Mean ± SD*

Amisulpride (n=0)	–	–	–	–
Aripiprazole (n=1)	2.2	2.0	1.5	1.8
Ziprasidone (n=2)	253.0 ± 21.2	246.0 ± 8.5	235.5 ± 0.7	231.0 ± 1.4
Clozapine (n=0)	–	–	–	–
Quetiapine & Quetiapine XR (n=7)	52.4 ± 83.5	57.2 ± 91.8 (2)	51.8 ± 85.5 (1)	43.6 ± 69.5
Olanzapine (n=1)	24.1	–	–	23.0
Paliperidone (n=0)	–	–	–	–
Risperidone (n=0)	–	–	–	–
Other Antipsychotic (n=0)	–	–	–	–

Table 32 Mean change (and 95%CI) of total cholesterol from first to final study visit

Scale / measurement	Current therapy	N	Mean Change V4-V1	Lower 95% CI	Upper 95% CI	p–value
Total Chol. (mmol/L)	Ziprasidone	2	–22.00	–199.89	155.89	NA
	Quetiapine & Quetiapine XR	7	–8.79	–21.74	4.17	0.148

Table 33: Patients' LDL cholesterol levels at each study visit*

Current antipsychotic therapy, (n=8)	LDL Cholesterol (mmol/L)			
	Visit 1 *Mean ± SD*	**Visit 2** *Mean ± SD*	**Visit 3** *Mean ± SD*	**Visit 4** *Mean ± SD*
Amisulpride (n=0)	–	–	–	–
Aripiprazole (n=1)	1.3	1.3	1.0	1.3
Ziprasidone (n=2)	204.5 ± 4.9	187.0 ± 9.9	181.5 ± 10.6	172.5 ± 17.7
Clozapine (n=0)	–	–	–	–
Quetiapine & Quetiapine XR (n=5)	39.2 ± 59.4	53.3 ± 79.5	58.4 ± 88.1	43.1 ± 71.1
Olanzapine (n=0)	–	–	–	–
Paliperidone (n=0)	–	–	–	–
Risperidone (n=0)	–	–	–	–
Other Antipsychotic (n=0)	–	–	–	–

Table 34 Mean change (and 95%CI) LDL cholesterol from first to final study visit.

Scale / measurement	Current therapy	N	Mean Change V4-V1	Lower 95% CI	Upper 95% CI	p–value
LDL (mmol/L)	Ziprasidone	2	–32.00	–146.36	82.36	NA
	Quetiapine & Quetiapine XR	5	3.97	–10.74	18.69	0.495

Table 35 Patients' HDL cholesterol levels at each study visit*

Current antipsychotic therapy, (n=10)	HDL Cholesterol (mmol/L)			
	Visit 1 *Mean ± SD*	**Visit 2** *Mean ± SD*	**Visit 3** *Mean ± SD*	**Visit 4** *Mean ± SD*
Amisulpride (n=0)	–	–	–	–
Aripiprazole (n=1)	34.8	35.9	37.0	40.2
Ziprasidone (n=2)	47.5 ± 17.7	54.0 ± 5.7	52.5 ± 7.8	57.0 ± 14.1
Clozapine (n=0)	–	–	–	–
Quetiapine & Quetiapine XR (n=6)	29.9 ± 15.8	29.6 ± 19.8	30.5 ± 19.8	33.6 ± 16.9
Olanzapine (n=1)	65.0	–	–	60.0
Paliperidone (n=0)	–	–	–	–
Risperidone (n=0)	–	–	–	–
Other Antipsychotic (n=0)	–	–	–	–

Table 36 Mean change (and 95%CI) of HDL cholesterol from first to final study visit

Scale / measurement	Current therapy	N	Mean Change V4-V1	Lower 95% CI	Upper 95% CI	p–value
HDL (mmol/L)	Ziprasidone	2	9.50	–276.39	295.39	NA
	Quetiapine & Quetiapine XR	6	3.76	0.27	7.25	0.039

Table 37 Patients' Triglycerides levels at each study visit*

Current antipsychotic therapy, (n=10)	Triglycerides (mmol/L)			
	Visit 1 *Mean ± SD*	**Visit 2** *Mean ± SD*	**Visit 3** *Mean ± SD*	**Visit 4** *Mean ± SD*
Amisulpride (n=0)	–	–	–	–
Aripiprazole (n=1)	2.3	1.9	6.6	14.9
Ziprasidone (n=2)	370.0 ± 282.8	321.0 ± 224.9	270.0 ± 169.7	236.0 ±132.9
Clozapine (n=0)	–	–	–	–
Quetiapine & Quetiapine XR (n=7)	71.1 ± 93.5	97.2 ± 98.3 (2)	74.4 ± 95.7 (1)	62.4 ± 84.0
Olanzapine (n=0)	–	–	–	–
Paliperidone (n=0)	–	–	–	–
Risperidone (n=0)	–	–	–	–
Other Antipsychotic (n=0)	–	–	–	–

Table 38 Mean change (and 95%CI) of Triglycerides from first to final study visit.

Scale / measurement	Current therapy	N	Mean Change V4-V1	Lower 95% CI	Upper 95% CI	p–value
Triglycerides (mmol/L)	Ziprasidone	2	–134.00	–1480.86	1212.86	NA
	Quetiapine & Quetiapine XR	7	–8.64	–18.39	1.12	0.073

Table 39 Patients' prolactin levels at each study visit*

Current antipsychotic therapy, (n=39)	Prolactin (ng/ml)			
	Visit 1 *Mean ± SD*	**Visit 2** *Mean ± SD*	**Visit 3** *Mean ± SD*	**Visit 4** *Mean ± SD*
Amisulpride (n=0)	–	–	–	–
Aripiprazole (n=5)	118.6 ± 55.3	76.6 ± 62.6	51.8 ± 39.9 (1)	23.2 ± 11.3
Ziprasidone (n=0)	–	–	–	–
Clozapine (n=2)	95.7 ± 119.7	64.9 ± 49.4	37.5 ± 38.9	16.2 ± 8.8
Quetiapine & Quetiapine XR (n=22)	67.4 ± 34.5	40.0 ± 23.6	25.3 ± 14.5	21.0 ± 9.4
Olanzapine (n=7)	98.9 ± 57.9	50.0 ± 28.6	46.6 ± 31.5	20.6 ± 16.5
Paliperidone (n=2)	75.8 ± 18.0	60.3 ± 28.6	36.4 ± 5.9	19.4 ± 6.9
Risperidone (n=0)	–	–	–	–
Other Antipsychotic (n=1)	149.4	122.0	–	38.0

Table 40 Mean change (and 95%CI) in prolactin from first to final study visit.

Scale / measurement	Current therapy	N	Mean Change V4-V1	Lower 95% CI	Upper 95% CI	p–value
Prolactin	Aripiprazole	5	–95.39	–156.73	–34.04	0.012
(ng/ml)	Clozapine	2	–79.45	–1076.25	917.35	NA
	Quetiapine & Quetiapine XR	22	–46.42	–60.07	–32.76	<0.0001
	Olanzapine	7	–78.36	–126.85	–29.87	0.008
	Paliperidone	2	–56.40	–280.03	167.23	NA

Compliance

Compliance to treatment was evaluated by the use of patient BARS scores at each study visit. **Table 42** indicates that the mean BARS scores increased from the first to final visit for all therapeutic agents.

Table 41 Patients' BARS scores at each study visit

Current antipsychotic therapy, (n=568)	BARS			
	Visit 1 *Mean ± SD*	**Visit 2** *Mean ± SD*	**Visit 3** *Mean ± SD*	**Visit 4** *Mean ± SD*
Amisulpride (n=23)	79.6 ± 25.3	90.7 ± 12.2	92.4 ± 9.5	92.7 ± 9.1
Aripiprazole (n=56)	90.4 ± 16.9	95.6 ± 9.7	96.3 ± 8.3	96.7 ± 7.5
Ziprasidone (n=26)	90.0 ± 22.4	93.8 ± 10.9	94.4 ± 11.7	95.3 ± 11.4
Clozapine (n=13)	78.1 ± 20.2	91.5 ± 10.1	96.9 ± 6.0	96.5 ± 5.9
Quetiapine & Quetiapine XR (n=318)	85.5 ± 17.2	92.5 ± 11.3	95.0 ± 9.0	95.5 ± 9.1
Olanzapine (n=47)	85.7 ± 20.9	95.8 ± 7.7	97.6 ± 5.2	97.5 ± 5.2
Paliperidone (n=35)	91.7 ± 15.8	98.5 ± 3.8	98.7 ± 4.1	98.4 ± 5.5
Risperidone (n=34)	82.3 ± 19.0	91.3 ± 12.8	94.9 ± 8.0	96.3 ± 7.1
Other Antipsychotic (n=16)	89.4 ± 13.0	92.2 ± 9.8	93.5 ± 13.0	93.2 ± 10.6

Table 42 Mean change (and 95%CI) of BARs from first to final study visit.

Scale / measurement	Current therapy	N	Mean Change V4-V1	Lower 95% CI	Upper 95% CI	p–value
BARs	Amisulpride	23	13.13	4.54	21.72	0.004
	Aripiprazole	56	6.30	2.64	9.97	0.001
	Ziprasidone	26	5.38	–3.26	14.03	0.211
	Clozapine	13	18.46	5.86	31.06	0.008
	Quetiapine & Quetiapine XR	318	9.95	8.27	11.62	<0.0001
	Olanzapine	47	11.83	5.88	17.78	<0.0001
	Paliperidone	35	6.71	1.53	11.90	0.013
	Risperidone	34	14.03	7.67	20.39	<0.0001
	Other Antipsychotic	16	3.81	–3.25	10.88	0.268

10. SAFETY

Due to the non-interventional nature of this study, no pro-active safety data collection was present.

11. ETHICS

Ethical approval

Prior to the start of study conduct, the protocol and written subject consent form was reviewed and accepted by the Scientific Committee/Administrative Council (IRBs) of the participating hospitals, as well as by the Greek National Organization of Medicines (ΕΟΦ). Signed and dated approval statements from the Hospitals' Scientific Committee/Administrative Council and ΕΟΦ were sent to AstraZeneca SA prior to study initiation.

Written consent

As per the protocol, the investigators ensured that each patient received accurate and comprehensive oral and written information about the nature, purpose, possible risks and benefits of the presented study, prior to the performance of any study-related procedure.

Patients were also notified that they were free to discontinue their participation in the study at any time and for any reason. The patient was given the opportunity to ask questions about the nature and purpose of the study and all study-related procedures, as well as time for consideration. Signed informed consent forms (ICF) were obtained in duplicate before enrolling the patient into the study. The original signed ICFs are kept by the investigator and a copy was given to the patient.

Study conduct

Investigators were responsible for compliance with the protocol. By signing the protocol, the Investigator agreed to abide by the guidelines and procedures described in the protocol and the Declaration of Helsinki (guiding principles of ICH/GCP) for the protection of human rights, and all applicable national and EU rules and regulations.

12. DATE OF THE REPORT

January 31st, 2011

13. REFERENCES

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