STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: Seroquel®
ACTIVE INGREDIENT: Quetiapine fumarate

Study No: NIS-NES-SER-2006/1
Titlle: **Adherence in adolescents and children treated with quetiapine**

Developmental phase: Phase – IV
Study Completion Date: April-2009
Date of Report: June - 2009

OBJECTIVES:

1   **Primary objective:** Survival analysis of adherence to treatment with quetiapine (Time frame: 6 months)

2   **Secondary objectives:**

   2.1   Survival analysis of adherence to treatment with quetiapine (Time frame: 12 months)

   2.2   Sociodemographic and clinical parameters (CGI-C, CGI-Suicidal, PANSS, HDRS, YMRS, SDQ, DAS, GAF, SUMD) possibly influencing on adherence (Time frame: 0, 6, 12 months)

   2.3   Tolerability profile (UKU) possibly influencing on adherence (Time frame: 0, 6, 12 months)

METHODS:

- **Study design:**

   Observational, retrospective (looking back) and single group (case only) study aimed to describe the adherence in a population of adolescents and children treated with quetiapine due to psychotic symptons, and to identify predictive factors influencing on the adherence to treatment with Quetiapine.

- **Target subject population:**

   Children and adolescents with psychosis in outpatients setting on treatment with quetiapine started from August 2005 to February 2008.

- o **Inclusion criteria:**

    1. At least one psychotic symptom (delusions or hallucinations) before the age of18.

    2. Start of treatment in a maximum period of 2 years after the onset of first psychotic symptom.

    3. Written informed consent by parents or guardians and patients.

- o **Exclusion criteria:**

    1. Pregnancy or lactating

    2. High risk of aggression or suicidal behaviour

    3. Alcohol dependence

- **Statistical methods:**

    The response variable was continuation/discontinuation (binary variable) of treatment with quetiapine for a 6-month-period. The explanatory variables included: age, gender, race, length of mental illness, previous treatment with antipsychotic, GAF at baseline, BMI at baseline, adverse events (on the first 15 days), involuntary movements (extrapiramidal symptoms) at baseline, substance abuse (tobacco, alcohol, cannabis, cocaine, opioids and synthesis drugs).

    Each variable was summarized using standard summary statistics. It was carried out a bivariate analysis to examine associations between response variable and each of explanatory variables. Then a Cox regression was used to assess the relationship between response variable and explanatory variables.

    Due to shortage of data, the analysis treatment for 12 months and the psychometric assessment were not carried out.

RESULTS:

- **Subject population:**

    61 patients, 64% male (n=39) and 36% female (n=22), were included. Mean (SD) age was 16.3 (1.0). 68.9% (n=42) of patients continued with quetiapine for 6 months.
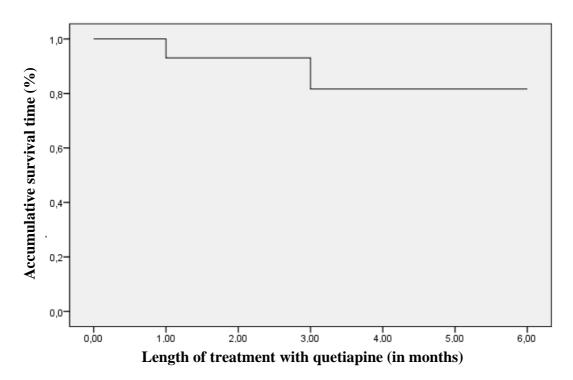
    All patients who were treated with Quetiapine for 6 months or longer, have a main diagnosis of psychosis, including: schizophrenia, bipolar, schizoaffective, schizophreniform and brief psychotic disorders. On the other hand, 7 out of 19 patients who were treated with quetiapine for less than 6 months, had another main diagnosis: obsessive-compulsive disorder (n=4) or eating disorder (n=3) (p=0.007).

- **Clinical results:**

Extrapiramidal symptoms were more frequent at baseline, in the group of patients who were treated with quetiapine for less than 6 months (p=0.021). Only this variable showed a statistically significant relationship with the response variable (continuation/discontinuation of treatment with quetiapine for 6 months) in the Cox regression analysis (Hazard ratio= 8.3; p= 0.007).

TABLE 1. BIVARIATE ANALYSIS				
	TOTAL N=61	**≥6 MONTHS OF TREATMENT N=42**	**<6 MONTHS OF TREATMENT N=19**	**STATISTICAL RESULTS**
Age: mean (SD, CI)	(N=61) 16.3 (1.0, 14-18)	(N=42) 16.3 (0.9, 14-17)	(N=19) 16.2 (1.1, 15-18)	U Mann-Whitney p=0.615
Gender (V:M)	(N=61) 39:22	(N=42) 27:15	(N=19) 12:7	Chi-square p=0.932
Naive	(N=61) N=16	(N=42) N=10	(N=19) N=6	Chi-square p=0.523
Caucasian race	(N=61) N=53	(N=42) N=35	(N=19) N=18	Chi-square p=0.222
Psychosis	(N=61) N=57	(N=42) N=42	(N=19) N=15	Fisher p=0.007
Length of illness: mean (SD, CI) in weeks	(N=11) 14.7 (11.7, 1-32)	(N=7) 12.1 (11.4, 1-32)	(N=4) 19.3 (12.3, 1-28)	U Mann-Whitney p=0.527
GAF at baseline: mean (SD, CI)	(N=18) 63.5 (11.7, 40-85)	(N=16) 61.8 (10.8, 40-80)	(N=2) 77.5 (10.6, 70-85)	U Mann-Whitney p=0.078
BMI: mean (SD, CI)	(N=49) 21.0 (3.0, 15.2-32.4)	(N=35) 21.3 (3.1, 16.1-32.4)	(N=14) 20.3 (2.8, 15.2-25.7)	U Mann-Whitney P=0.330
Last visit: 6 months 3 months 1 months	N=42 N=6 N=13	N=42 N=0 N=0	N=0 N=6 N=13	
Tobacco use	(N=60) N=26	(N=41) N=18	(N=19) N=8	Chi-square p=0.896
Cannabis use	(N=60) N=24	(N=41) N=16	(N=19) N=8	Chi-square p=0.821
Cocaine use	(N=60) N=2	(N=41) N=2	(N=19) N=0	Fisher p=1.000
Alcohol use	(N=60) N=19	(N=41) N=15	(N=19) N=4	Fisher p=0.371
Synthesis drugs	(N=60) N=4	(N=41) N=4	(N=19) N=0	Fisher p=0.297
Opioids use	(N=60) N=0	(N=41) N=0	(N=19) N=0	
Substance abuse (general)	(N=60) N=28	(N=41) N=20	(N=19) N=8	Chi-square p=0.630
UKU positive	(N=27) N=10	(N=20) N=9	(N=7) N=1	Fisher p=0.204
Dystonia	(N=34) N=9	(N=27) N=7	(N=7) N=2	Fisher p=1.000
EPS	(N=34) N=4	(N=27) N=1	(N=7) N=3	Fisher p=0.021
Akathisia	(N=34) N=0	(N=27) N=0	(N=7) N=0	

FIGURE 1.

Survival analysis (COX regression)

Y-axis: **Accumulative survival time (%)** (1,0 — 0,8 — 0,6 — 0,4 — 0,2 — 0,0)

X-axis: **Length of treatment with quetiapine (in months)** (0,00 — 1,00 — 2,00 — 3,00 — 4,00 — 5,00 — 6,00)