AstraZeneca

# D1449L00003

**SUMMARY**

**ASTRAZENECA PHARMACEUTICALS**

**FINISHED PRODUCT:** Seroquel

**ACTIVE INGREDIENT:** Quetiapine

**Trial title**: Fast Titration of Quetiapine versus Currently Approved Titration: A Randomized, Multicentre, Parallel Group, Open Trial in Schizophrenia and Schizoaffective Disorder.

**Developmental phase:** IIIb
**First subject recruited:** October 2004
**Last subject completed:** September 2005
**Approval date:** N/A

**OBJECTIVES**

The primary objective was to compare the safety and tolerability of a fast titration of quetiapine versus the current titration approved by the Regulatory Authorities for the treatment of schizophrenia.

The secondary objectives were:

1. Assess changes from baseline in Vital Signs after intake of quetiapine.
2. Assess the clinical efficacy of a fast titration of quetiapine versus the current titration approved by the regulatory authorities for the treatment of schizophrenia.

**METHODS**

**Study design**

This was a multicentre, randomised, parallel group open trial of two different titration schemes of quetiapine: Group A = Fast titration, Group B = Currently approved titration. Eligible subjects were randomly assigned to Group A or Group B in a ratio of 1:1.

**Target subject population**

Patients with acute exacerbation of schizophrenia or schizoaffective disorder (according to DSM-IV criteria) requiring hospitalisation and with a CGI (Clinical Global Impression) severity score $\geq$4. The patients should stay in hospital for a minimum of the first 7 days of the study period.

**Investigational product, dosage and mode of administration**

Quetiapine administered twice daily according to a fast titration scheme in a 4 days period (200 mg/day Day 1; 400 mg/day Day 2; 600 mg/day Day 3; 800 mg/day Day 4) = GROUP A.

**Comparator, dosage and mode of administration**

Quetiapine administered twice daily according to the currently approved titration scheme in a 4 days period (50 mg/day Day 1; 100 mg/day Day 2; 200 mg/day Day 3; 300 mg/day Day 4; 400 mg/day Day 5) = GROUP B.

**Duration of treatment**

14 days

**Outcome variables**

**Safety**

**Primary outcome variable:**

- Proportion of patients with moderate and severe adverse events day 2 to day 5.

**Secondary outcome variables:**

- Mean daily level of somnolence day 2 to day 5 according to AE intensity scale.
- Mean daily level of orthostatic dizziness day 2 to day 5 according to AE intensity scale.
- Proportion of patients developing abnormal ECG patterns.
- Dropouts due to adverse events by end of week 1 as well as total adverse events end of week 1.
- Decreases in systolic BP of $\geq$20mmHg or decreases in diastolic BP of $\geq$10mmHg and increases in pulse rates $\geq$30 bpm.
- Post-baseline supine pulse rate $\geq$120 bpm and a change from baseline of $\geq$20 bpm

**Efficacy**

**Secondary outcome variable:**

- Changes from baseline PANSS (Positive And Negative Symptom Scale) and CGI (Clinical Global Impression) Severity of Illness scale.
- Number of subjects with CGI Global Improvement ratings at “much improved” and “very much improved”.

**RESULTS**

The study was planned with the inclusion of 150 patients, but only 10 patients were enrolled. No statistical tests were used, as too few patients were included. Patient Nos 8-10 were randomized to fast titration (group A), patient Nos 1-7 to regular titration (group B). Patients 1, 3, 4, 5, 6, 7, 10 had schizophrenia, patients 2, 8, 9 had schizoaffective disorder. All patients followed the titration schedule, except patient 7 on Day 4 and 5 (Day 1 50 mg, Day 2 100 mg, Day 3 200 mg, Day 4 500 mg, Day 5 200 mg). Patient Nos. 1, 4, 5 and 9 discontinued the study (No. 4 stopped taking the medication); No. 1 after Visit 2, No. 4 after Visit 6, No. 5 &9 after Visit 4. One patient had moderate or severe AEs day 2-5 after dosing in the fast titration group and two patients had such AEs in the current titration group (primary endpoint). It is not possible to draw conclusions from the present study as it was terminated prematurely; i.e. before 10 % of the planned patients were included