SYNOPSIS

Name of Sponsor/Company:	Janssen-Cilag, S.A.
Name of Finished Product:	Risperidone
Name of Active Ingredient(s):	Risperidone

Protocol No.: CR009313

Title of the study: Study on the safety of risperidone on obese or overweight patients with schizophrenia.

Coordinating Investigator(s): J. A. Fernández Benítez

Publication (Reference): None (Poster in a local Congress)

Study Initiation/Completion Dates: 2 July 2001/ 31 January 2003	**Phase of Development:** 4

Objectives: The primary objective was to evaluate safety of risperidone in patients with overweight and/or obesity. Secondary objective was to describe adherence and compliance to risperidone in psychotic patients diagnosed of schizophrenia (DSM-IV) .

Methodology: This was a six-month, multi-centre, open, prospective design study that describes the clinical profile of patients with schizophrenia and schizoaffective disorders with a BMI >25, patients who have increased their body weight >7% in the last year, with the previous treatment, or have shown intolerance to a previous antipsychotic treatment. The data was collected prospectively and it included demographic data, psychiatric history and co morbidities, concomitant medications, body weight, treatment history and other illness related to obesity (such as diabetes mellitus I y II, hypertension and hypercholesterolemia) and adverse events.

Number of Subjects (planned and analyzed): It was planned that 1500 consenting patients, that fulfill the inclusion criteria were enrolled in the study, in Spanish selected centers. A total of 1717 patients were finally eligible to participate, 1298 patients completed the study and 419 drop out. 1261 patients were included in the efficacy analysis and 1717 were included in the safety analysis.

Diagnosis and Main Criteria for Inclusion: Male and female, ≥ 18 years of age with schizophrenia or schizoaffective disorder, a BMI >25, patients who have increased their body weight >7% in the last year with the previous treatment or have shown intolerance to a previous antipsychotic treatment.

Test Product, Dose and Mode of Administration, Batch No.: This was a descriptive study carried out according to the general clinical practice. Therefore, no intervention in the prescribed drugs was performed.

Reference Therapy, Dose and Mode of Administration, Batch No.: Non applicable.

Duration of Treatment: The follow up period was 6 months

SYNOPSIS (CONTINUED)

Criteria for Evaluation:

Efficacy: The primary efficacy endpoint variable of this study was the body weight measure in basal, 2 months, 4 months and 6 month (final) visits. Also BMI evolution was measure in all visits. The secondary efficacy analyses were to describe the compliance and adherence of patients to treatment. BPRS, MARS (adherence to treatment), EEAG (compliance) and EVA (patient's treatment compliance and physician's

treatment compliance) scales were used.

Safety: The assessment of safety was mainly based on elicited adverse events. Special emphasis was given to EPS (extrapyramidal symptoms) measure by UKU scale and anticholinergic or sedative effect of the treatment.

Statistical Methods: Changes in body weight, BMI and BPRS, EEAG and EVA scales scores were analyzed using analysis of variance (ANOVA). Categorical variables were summarized by presenting the corresponding confidence interval of 95% (CI 95%).

Adverse events were coded using a Medical Dictionary for Regulatory Activities. Safety results were analyzed using descriptive statistic.

SUMMARY – CONCLUSIONS

EFFICACY RESULTS:

In ITT analysis, a total of 1261 patients, treated with risperidone have reduced their body weight (kg) from a basal mean of 83.65 ± 13.28 to final mean of 80.34 ± 12.57 ($p < 0,001$) after 163.68 days of treatment. Progression of BMI was from a basal mean of 29.44 ± 4.08 to a final mean of 28.30 ± 3.84 ($p< 0,0001$).

BPRS scale variation: basal mean score: 25.22 ± 11.34 and final mean score: 12.29 ± 8.05 ($p< 0,0001$).
EEAG scale variation: basal mean 46.95 ± 14.91 and final mean score was 64.88 ± 14.39 ($p<0,0001$).
EVA scale (compliance of patients) was from 36.26 ± 20.52 to 67.74 ± 19.37 ($p<0,0001$) and physician compliance was from 39.60 ± 20.31 to 74.16 ± 16.18 ($p< 0,0001$).

SAFETY RESULTS:

1717 patients were included in the safety analysis. 4.08% of the study population (70 patients) suffered 104 non serious AEs during the study (61 were mild, 38 were moderate and 3 were severe). 42 patients experienced serious adverse events (0,02%). One patient committed suicide (the investigator responsible considered this SAE not related to risperidone treatment; the patient has a diagnostic of psychotic disorder and bipolar disorder type I).
Mean dose used to treat during the study was 5.83 ± 2.49 mg/day.

SYNOPSIS (CONTINUED)

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Date of the report: 7th of September 2007