SYNOPSIS

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

Protocol No.: RIS-PSI-AGUDOS-02-02 (CR009214)

Title of the study: Impact of aggressiveness/agitation in response and safety to risperidone in acute psychotic patients.

Coordinating Investigator(s): Dr. Miguel Lázaro (Hospital Universitario Son Dureta)

Publication (Reference): None

Study Initiation/Completion Dates: 29-Nov-2001/ 22-Aug-2002 | **Phase of Development:** 4

Objectives: The aim of this study was to evaluate the safety of risperidone treatment in acute psychotic patients that require an admission into a hospital. The effectiveness of risperidone controlling acute psychotic symptomatology and incidence, severity and risk of psychomotor agitation in acute psychotic patients was studied, too.

Methodology: This was a six-months, multi-centre, open, prospective design study describing the clinical profile of patients with schizophrenia and schizoaffective disorders with acute psychotic symptoms that required an admission into a hospital and in which physicians considered the use of risperidone as treatment under clinical practice.
All data collected will be prospective and will include the following: demographic and clinical data, safety data (UKU and CGI scales) and effectiveness data (PANNS and BPRS).

Number of Subjects (planned and analyzed): It was planned that approximately 1250 consenting patients satisfying the inclusion criteria were to be enrolled in the study from selected centers in Spain. Finally, a total of 1882 patients were eligible to participate, 1837 patients completed the study and 45 abandon. A total of 1740 patients were including in the efficacy analysis and 1882 were including in the safety analysis.

Diagnosis and Main Criteria for Inclusion: Males and females ≥ 18 years of age with Acute Psychotic symptoms in Schizophrenia; Schizoaffective disorder and Schizophreniform disorder in patients that required an admission into a Hospital and in which physicians considered the use of risperidone as treatment under clinical practice.

Test Product, Dose and Mode of Administration, Batch No.: Risperidone, 3-6 mg/day, orally.

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

Duration of Treatment: during in-patient period

SYNOPSIS (CONTINUED)

Criteria for Evaluation:

Safety: The assessment of safety was mainly based on adverse events. Special emphasis was given to EPS (extrapyramidal symptoms) measure by UKU scale and anticholinergic symptoms and sedative level measured by CGI scale. Scales should be filled in the first day of the admission, 3 days after admission and

the day that the patient leaves the Hospital.

Effectiveness: In the effectiveness analyses were used BPRS scales and the PANNS agitation sub-scale. Scales should be filled in the first day of the admission, 3 days after admission and the day that the patient leaves the Hospital.

Statistical Methods: Statistical analysis was performed by SPSS program v 9.0. The evolution of the disease severity grade during the study was evaluated by BPRS, PANSS and visual analogical scales using Wilcoxon test to compare between two visits and Friedman test to compare all visits. SOAS scale was analyzed by Chi-square test (CI 95%).

SUMMARY – CONCLUSIONS

Effectiveness results

BPRS scale: basal mean of 33.45 ± 10.49 to final mean of 10.58 ± 7.61 ($p<0.0001$) after 17.82 days of treatment. PANSS scale: basal mean 4.24 ± 1.79 to final mean 1.40 ± 0.71 points ($p<0.0001$). SOAS scale provocation item: 37.16% patients (basal visit) to 3.26% patients (final visit) ($p<0.0001$). Visual analogical scale has showed a decrement in the score of the agitation parameter (from 46.27 ± 29.63 to 6.46 ± 11.08) as well in anxiety (from 56.95 ± 25.10 to 11.92 ± 13.56) ($p<0,05$). Mean dose of risperidone dispensed during the study was 7.01 ± 3.36 mg/day.

Safety results

173 adverse reactions have been development in 119 patients (6.32%). The percentage of patients that didn't receive antiparkinsonism medication during the follow up period has been decreased (from 76.54% to 68.82%) ($p<0.0001$). Total score in Sedation CGI scale has been reduced (from 2.15 ± 1.36 to 1.79 ± 0.91) during the follow up ($p<0.0001$). 5 patients (0.27%) experienced serious adverse event.

SYNOPSIS (CONTINUED)

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Mean dose of risperidone during the study was 7.01 ± 3.36 mg/day.

Date of this report: the 09th of July 2007

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