SYNOPSIS

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

Protocol No.: CR 010609

Title of the study: Study PROFIL*e*3: Clinical observations profile of relapse and readmission in emergency/acute settings: Epidemiological survey in schizophrenic patients.

Coordinating Investigator(s): Miquel Bernardo Arroyo, M.D. (Hospital Clínic, Barcelona, Spain) and Luis San Molina, M.D. (Hospital San Rafael, Barcelona, Spain).

Publication (Reference): None

Study Initiation/Completion Dates: 1 April 2005 - 30 September 2005	**Phase of Development:** 4

Objectives: The purpose of this study was to evaluate epidemiological characteristics of patients that experienced relapse and needed an admission in psychiatric acute units across Spain. The specific objectives of the study were to determine the most important risk factors which predict the number of hospital readmissions (predictor and protective variables), and to identify the clinical profile of patients with schizophrenia and schizoaffective/schizophreniform disorders who suffer relapses (predictive model). The secondary objective of the study was to describe the clinical decisions taken by the psychiatric doctors regarding therapeutic approach according to the previous characteristics of the patient.

Methodology: This was a six-month, multi-centre, cross-sectional-retrospective design study describing the clinical profile of patients with schizophrenia and schizoaffective disorders with more than 2 years of evolution, who were admitted in short-stay psychiatric hospitalization units or acute units at the time of the inclusion visit. The patients were divided in 2 cohorts based on their history of prior hospital admissions within the last 3 years: The Case group comprised the patients with prior hospitalizations and <24-month evolution periods, whereas the Control group contained those patients without prior hospitalizations or with at least one >24-month evolution period between two successive admissions. The duration of the recruiting period was 3 months for each participating centre.

Number of Subjects (planned and analyzed): It was planned that approximately 2000 consenting patients satisfying the inclusion criteria were to be enrolled in the study from selected centres in Spain. Finally, a total of 1607 patients were eligible to participate and were assigned on the basis of their frequency of hospital admissions within the last 3 years into the Case (N=656) and Control (N=951) groups.

Diagnosis and Main Criteria for Inclusion: Males and females, with schizophrenia or schizoaffective disorder, with a disease history over 2 years, who were hospitalized in a short-stay psychiatric hospitalization unit or an acute unit. Patients with psychiatric pathology other than schizophrenia or schizoaffective disorder were excluded from the study, as well as those with a disease history of less than 2 years.

Test Product, Dose and Mode of Administration, Batch No.: This was a descriptive study carried out according to the general clinical practice. Therefore, any 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 comprised the 3 previous years of the inclusion date.

SYNOPSIS (CONTINUED)

Criteria for Evaluation:

Efficacy: The primary efficacy endpoint variable of this study was the occurrence of relapses/readmissions within the last 3 years associated with possible predictor variables. The secondary efficacy analyses were to describe the profile of patients prone to schizophrenic disease remissions according to socio-demographic data (age, sex, race, nationality, education level, socio-economic level, familial support, rural/urban area); diagnosis (type of schizophrenic disorder, severity); psychiatric history, comorbidities and hospitalization history (years of disease evolution, substance abuse, stress factors and toxic abuse associated with relapses, main reason for admission); treatment history (pharmacological and non-pharmacological, before and during hospitalizations); and physician's opinion on patient's treatment compliance.

Safety: The assessment of safety was mainly based on adverse events. Special emphasis was given to severe adverse events associated with the pharmacological therapy that caused the interruption of the treatment.

Statistical Methods: Continuous variables were described by presenting the following summary statistics: number of patients with non-missing values (n), mean, standard deviation (SD), median, minimum and maximum. Categorical variables were summarized by presenting the number of patients, the percentage for each category and the corresponding confidence interval of 95% (CI 95%).

Those variables associated to the patient's relapses and hospital admissions were identified through univariate logistic regression, and were subsequently subjected to multivariate analysis to eventually assess the predictor/protective factors of hospitalization. A signification level of 0.05 was considered for all the statistical tests. Statistical analyses were performed using SAS version 8.2.

SUMMARY – CONCLUSIONS

EFFICACY RESULTS:

Clinical profile of patients at short-stay hospitalization units: The socio-demographic profile of patients with frequent relapses in relation to controls revealed an older age, lower education/socio-economic level, more presence in rural environments, less familial support and increased toxic abuse. Their clinical history showed a lower percentage of schizophreniform disorders but a higher presence of schizoaffective disorders. Stressful familial events and tobacco consumption were more prevalent in this group, as well as the incompliance of treatment, the main cause of psychotic relapse.

Due to their worse condition, case subjects used to receive both non-pharmacological and pharmacological treatment in a higher proportion than control patients, with significant differences for day care centre, psycho-educative support, psycho-social therapy, and the antipsychotic medications amisulpride, quetiapine fumarate, risperidone and zuclopentixol.

Predictor factors for high readmission rates (cases): The predictor factors determined by logistic regression analysis (schizoaffective disorder, adherence, smoking, day care centre, amisulpride, risperidone, zuclopentixol and stressful events) allowed developing a multivariate model.

SAFETY RESULTS:

A total of 115 studied patients (a 7.2% of the overall sample) experienced one or more adverse events, with similar incidence in both groups. The most frequent affected the nervous system, musculoskeletal and connective tissue, and the gastrointestinal tract (respectively 4.3%, 0.9% and 0.8% overall). Only 4 patients suffered one severe adverse event, 2 subjects of each group, but no deaths occurred in the course of the

study.

SYNOPSIS (CONTINUED)

CONCLUSION:

The socio-demographic and clinical profile of schizophrenic patients prone to suffer disease remissions has been described, and the predictor variables identified. Furthermore, the multivariate model developed in this study could be very useful to predict future hospitalizations in schizophrenic patients.

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