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Sponsor/company:	sanofi-aventis	**ClinialTrials.gov Identifier:**	NCT00331981
		Study Code:	L_8968
Generic drug name:	Amisulpride	**Date:**	09/Jan/2008

Title of the study:	Study of the efficacy and safety of long-term treatment with Amisulpride in schizophrenic patients in Korea
Investigator(s):	Yong Sik Kim Address : Department of Psychiatry and Institute of Human Behavioral Medicine, Seoul National University College of Medicine, 28 Yongon-Dong, Chongro-Gu, Seoul, 110-799, Korea
Study center(s):	Republic of Korea Multicenter(7sites) study 1.YD-Cathoilic Medical Center 2.Seoul Medical Center 3.Seoul National Univ Hosp. 4.Severance Medical Center 5.Yongin Mental Hosp. 6.Inha Univ Hosp. 7.Chung-buk Univ Hosp.
Publications (reference):	NA
Study period: Date of study initiation: 01-Feb-2004 Date of study completion: 13-Aug-2005	**Phase of development:** Phase IV
Objectives:	To examine the efficacy and the safety of long-term use of amisulpride in Korean patients with schizophrenia.
Methodology:	12-month, open-label trial with flexible dose of amisulpride (50mg - 1200mg/day) at 7 sites in Korea. The effectiveness and safety during acute treatment phase (from baseline to 8 weeks) and delayed treatment phase (from 8 week to 12 month) were compared between 2 groups which were positive symptom dominant group and negative symptom dominant group based on baseline PANSS subscale scores. • Primary efficacy parameter : Positive and Negative Symptom Scale (PANSS), CGI-S and the GAF • Adverse events : Liverpool University Neuroleptic Side Effect Rating Scale (LUNSERS), and Drug-Induced Extra-pyramidal Symptoms Scale (DIEPSS)
Number of subjects:	Total number of subjects: 134 Efficacy evaluation subjects (ITT): 123 (6 patients: dropped out before post-baseline evaluation, 5 patients: not classified to which symptom dominant group because they had same scores of PANSS positive subscale and negative subscale.) • positive symptom dominant group: 48 • negative symptom dominant group: 75

Diagnosis and criteria for inclusion:	In- or out-patients, aged 18 to 65 years, were eligible for the study, who met the DSM-IV criteria of either schizophrenia or schizophreniform disorder. The subjects need antipsychotic treatment newly because of newly developed or aggravated psychotic symptoms, or need to switch other antipsychotic agents to amisulpride because of side effects and other reasons.
Investigational product:	Amisulpride
Dose:	Daily dose ranging from 50 to 1200 mg
Administration:	Oral administration
Duration of treatment: Two phases of treatment period : 1. acute treatment phase for the first eight weeks 2. chronic treatment phase from 8 weeks to 12 months	**Duration of observation:** This article reports the results of both 8-week acute treatment and 12-month chronic treatment.
Reference therapy:	NA
Dose:	NA
Administration:	NA
Criteria for evaluation:	
Efficacy:	• Primary effectiveness : total score and the positive and negative subscale scores of the Positive and Negative Syndrome Scale (PANSS) • Secondary effectiveness: Clinical Global Impressions (CGI) and the Global Assessment of Function (GAF).
Safety:	• Primary safety : DIEPSS, LUNSERS, drug related adverse event • Secondary safety: laboratory test results (serum prolactin level, ECG), Body weight and vital signs.
Statistical methods:	• Doses of amisulpride: Difference between positive symptom dominant group and negative symptom dominant group, the repeated measure ANOVA with only observed cases was used. • Efficacy & Safety analyses: performed based on the intent-to-treat (ITT) protocol with Last Observation Carried Forward (LOCF) method. • Primary & secondary effectiveness (PANSS in positive and negative dominant groups): paired t-test to test the difference in acute phase and delayed phase. The effects of treatment duration on the efficacy measures were also assessed using the repeated measures ANOVA with planned contrasts. The changes of scores on the CGI-S and the GAF were also tested using same methods. • Safety (DIEPSS and the LUNSERS): paired t-test with the changes at each treatment phases, as were the changes in laboratory test results. • All tests were performed by using two-tailed probabilities and set at a significance level of .05.

Summary:	The patients who have completed at week 8 and 12 month were 97 (78.9%) and 69 (56.1%), respectively. No significant differences in rate of completion at 8 week and 12 month were observed between positive and negative symptom dominant groups. Positive symptom dominant group showed the effectiveness in PANSS total, positive subscale and negative subscale scores only during acute phase treatment. However, negative symptom dominant group showed both acute effectiveness and delayed effectiveness in all primary effectiveness measures.
Efficacy results:	**1. Subjects Characteristics** • Mean age of the study population : 34.7 years • Mean age at onset: 26.7 years. • Patients completed at week 8 and 12 month: 97 (78.9%) and 69 (56.1%) **2. Prescribed dose of Amisulpride** 346.4 (± 173.2) mg/d and 273.2 (± 151.7) mg/d at baseline and 587.5 ± 323.5 mg/d and 447.6 ± 249.5 mg/d at 12 month in positive dominant and negative dominant group. The mean dose of positive symptom dominant group seemed to be higher than that in negative symptom dominant group without statistical significance **3. Efficacy Measures** • Positive symptom dominant group showed only acute effectiveness (PANSS total scores -17.1 ± 18.5 during first 8 weeks). • Negative symptom dominant group showed both acute effectiveness and delayed effectiveness (-17.5 ± 23.2 during acute phase treatment of PANSS total score and -3.1 ± 9.3 during delayed treatment phase of PANSS total score. The amount of decrease PANSS positive symptom subscale was greater than that in positive symptom dominant group during delayed phase (-0.8 ± 2.3 vs. 0.0 ± 4.4). • With repeated measure ANOVA, positive symptom dominant group showed the improvement of positive symptom occurred only within first 4 weeks but the improvement of negative symptom occurred only between 8 week and 16 weeks. Although negative symptom dominant group showed delayed improvement in both positive and negative symptom, further analysis at each visit showed improvement of negative symptoms only between 8 week and 16 week. • The improvement in CGI-S was observed during acute and delayed treatment phase in both groups. In positive symptom dominant group, the increase of GAF was observed only during acute phase but in negative dominant group, this increase was observed during both acute and delayed treatment phase.
Safety results:	• Of 123 patients, 88 (71.5%) experienced at least one adverse event during both treatment phase of amisulpride. Most of adverse events occurred during acute treatment phase and their rates were decreased at delayed treatment phase except for hyperprolactinemia and its related adverse events. • LUNSERS (114 patients who completed at least one post baseline evaluation) : The patients with amisulpride showed marked improvement in adverse events during early treatment phase but no further improvement was observed during late treatment phase. • DIEPSS: Improvement in extra-pyramidal symptom was marked during delayed treatment phase. Positive symptom dominant group showed similar pattern to overall subject with improvement of only delayed treatment phase, but negative symptom dominant group showed the significant improvement in both treatment phase. • Hyperprolactinemia (54 patients, 43.9%) was reported as the most common adverse event. (42.7ng/ml at the baseline, 92.7 ng/ml at 8 weeks, 73.3 ng/ml at 12-month)
Date of report:	06-Jul-2007