These results are supplied for informational purposes only. *Prescribing decisions should be made based on the approved package insert in the country of prescription*			
Sponsor/company:	sanofi-aventis	**ClinialTrials.gov Identifier:**	NCT00761670
Generic drug name:	Amisulpride	**Study Code:**	AMISU_L_01008
		Date:	2 December 2010

Title of the study:	Comparative efficacy of amisulpride vs. risperidone on cognitive functions in patients with chronic schizophrenia.
	Coordinating Investigator: Prof. Dr. István Bitter, M.D., Ph.D, D.Sc. Professor and Chair Department of Psychiatry and Psychotherapy Semmelweis University
Study center(s):	6 centers in Hungary 1.) Semmelweis University, Budapest (István Bitter, M.D., Ph.D, D.Sc.) 2.) Pándy Kálmán County Hospital, Gyula, (Gábor Vincze M.D., Ph.D.) 3.) University of Pécs ,(Sándor Fekete M.D., Ph.D, D.Sc) 4.) University of Debrecen, (Istvan Degrell M.D., PhD., D.Sc †., Assoc.Prof. Dr.Theodora Glaub) 5.) Bács-Kiskun County Hospital, (Oguz Kelemen M.D., Ph.D.) 6.) Dr.Kenessey Albert County Hospital, Balassagyarmat (László Csekey M.D.)
Publications (reference):	Preparation of manuscript for publication is currently under way.
Study period: Date first patient enrolled: 10-09-2008 Date last patient completed:15-01-2010	**Phase of development:** Phase IV

Objectives:	**Primary objectives** • To compare neurocognitive effects of amisulpride with those of risperidone in patients with chronic schizophrenia, as assessed by the general cognitive index, a measure of overall cognitive functioning in schizophrenia **Secondary objectives** • Secondary analyses were conducted to determine how the two atypical agents' neurocognitive effects compare with regard to their profile of therapeutic action (based on individual cognitive domain scores in seven cognitive domains, including speed of processing, attention/vigilance, working memory, verbal learning and memory, visual learning and memory, reasoning and problem solving and social cognition); • Investigate whether amisulpride elicits more improvement on negative symptoms compared to risperidone treatment, as measured by the total score on the SANS 8 and by the Negative Symptom Subscale of the PANSS; • Assess whether amisulpride improves overall functioning and individual domains of psychotic symptoms compared to risperidone as measured by the Clinical Global Impression (CGI), and the total and positive and general psychopathology subscale scores of PANSS and by the individual domains of SANS, respectively; Evaluate the safety and tolerability of amisulpride and risperidone based on the study completion rates, and frequency of abnormal laboratory values, prolactin serum concentrations and on the Simpson Angus Scale for Extrapyramidal Symptoms (SAS) 10 and the Abnormal Involuntary Movement Scale (AIMS).		
Methodology:	A randomized, open-label, comparator-controlled, parallel arm trial of 56 Days of treatment with amisulpride or risperidone		
Number of patients:	Planned: 102 (n=51/treatment arm)	Randomized: 37	Treated: 37
Evaluated:	Efficacy/Pharmacodynamics: Neurocognitive effect: 37 pts	Safety: 37 pts.	

Diagnosis and criteria for inclusion:	**Inclusion Criteria** 1. Diagnosis: DSM-IV schizophrenia (any subtype) 2. Aged between 18 and 65 years 3. Sex: Male, or non pregnant female subjects 4. General Health: Satisfactory medical assessment with no clinically significant and relevant abnormalities 5. Duration of illness: ≥ 5 years 6. Concomitant standing or prn medications (except other antipsychotics and those contraindicated in the respective package inserts [amisulpride or risperidone]) are permitted during treatment phase, if they were present at a stable dose for at least 6 weeks prior to the start of initial treatment with study medication 7. Overall symptom severity: patients must evidence a total score of 60 or higher on the PANSS scale 8. Clinical Symptoms: A score of 4 (moderate) or greater on any of the 7 items of the PANSS Positive Symptom Subscale (delusions, conceptual disorganization, hallucinatory behavior, excitement, grandiosity, suspiciousness/persecution, and hostility) is present 9. Cognitive status (minimum performance level): subject must be able to validly complete the baseline MATRICS assessment (validity of performance to be assessed by Chief Neuropsychologist or NP tester) 10. Clinical judgment by the investigator that treatments with amisulpride or risperidone are warranted due to suboptimal clinical outcome despite previous treatments 11. Patient is judged capable of understanding all relevant risks and potential benefits of the study and provides informed consent
Investigational product: Dose: Administration:	Amisulpride Patients were randomized in a 1:1 ratio to amisulpride or risperidone Target: 600 mg/day, The dose was variable depending on the patient's clinical condition, within the limit: 400-800 mg/day p.o. / tablet
Duration of treatment: 56 Days	**Duration of observation:** The total number of patients randomized for the trial was 37 (n=18 and 17 for the amisulpride and risperidone group, respectively). The duration of treatment was 8 weeks for the majority of patients in both groups; 1 patient in the amisulpride and 3 patients in the risperidone group, respectively, discontinued the study prematurely.
Reference therapy: Dose: Administration:	Risperidone Patients were randomized in a 1:1 ratio to amisulpride or risperidone Target: 6mg/day; The dose was variable depending on the patient's clinical condition, within the limit: 4-8 mg/day p.o. / tablet

Criteria for evaluation:	
Efficacy:	**Primary** General cognitive index, as assessed by the overall average z-score based on the neurocognitive test (MATRICS) battery. **Secondary** Cognitive measures: Individual subscales scores in seven cognitive domains including speed of processing, attention/vigilance, working memory (verbal and nonverbal), verbal learning and memory, visual learning and memory, reasoning and problem solving and social cognition. Overall Clinical Effects: Clinical Global Impression (CGI). Clinical Symptoms/Ratings of psychopathology: The total and each of the subscale scores on the PANSS (positive and negative symptoms, general psychopathology), and the SANS (Attention; Affect; Alogia, asociality/Anhedonia; Avolition). Ratings of potential side effects: The total, subscale and item scores on the Simpson-Angus Scale and the Abnormal Involuntary Movement Scale, respectively. General Safety/Tolerability: Completion rates and specific reasons for discontinuation, changes in vital signs, treatment-emergent adverse events, and frequency of abnormal laboratory measures. Prolactin serum concentrations.
Safety:	Measures included vital signs, laboratory assessments (including urinalysis and EKG), the Simpson Angus Scale for Extrapyramidal Symptoms (SAS) and the Abnormal Involuntary Movement Scale (AIMS). Adverse events, which were reported by the patients or observed by the Investigator, had to be recorded on the appropriate pages of the case report form. The Investigator had to immediately report all AEs, which he/she classifies as serious to the Pharmacovigilance Officer. In addition, the Investigator had to fill in an Adverse Event Form and the SAE Complementary Form. This form had to be sent to the Pharmacovigilance Officer as soon as possible but not later than 1 working day after the event**.**
Pharmacokinetics:	N/A (no pharmacokinetic data collected in study)
Statistical methods:	The primary efficacy analysis was based on the intent-to-treat approach, using data from all patients randomized for the trial. Data reduction for the analysis of neurocognitive test battery comprised the following steps: a) individual neurocognitive test scores at baseline (Day 0/Visit 2) and at Day 28/Visit 4 and Day 56 (End of Study/Early Termination/ Visit 5) were converted to z-scores using the formula: z = (individual score - overall baseline mean)/pooled baseline s.d.; b) z-scores within the pre-specified cognitive domains measured by more than one test were averaged to obtain a domain-specific z-score; and c) the overall average z-score for each participant at each testing occasion was calculated by averaging the domain-specific z-scores. The overall average z-score served as an index general cognitive functioning (General Cognitive Index), and was used as the primary endpoint for the trial. Difference between the treatments was tested by a mixed model for repeated measures (random-regression, hierarchical linear model [HLM]) and ANCOVA analyses. No interim analysis was performed**.** The alpha=0.05 level was adopted for statistical significance.

Summary:	
Efficacy results:	Both treatments elicited statistically significant improvement over time in the General Cognitive Index (p=0.0003 and 0.0085 for the amisulpride and risperidone groups, respectively). Improvement over time reached statistical significance (p<0.05) in 4 and 2 cognitive domains in the amisulpride and risperidone group, respectively. Due to the limited sample size, the difference between treatment groups in terms of improvement over time did not reach statistical significance. Neurocognitive domains with significant improvement included Processing Speed, Working Memory, Attention/Vigilance and Reasoning&Problem Solving for amisulpride, and Processing Speed and Attention/Vigilance for risperidone. Both treatments produced significant improvement in psychopathological measures, including PANSS and SANSS. The group difference in improvements was not statistically significant, with the exception of the PANSS cognitive factor where amisulpride treatment produced significantly more improvement than risperidone (p=0.047).
Safety results:	The proportion of discontinuations was 5.1% (1 of 19 patients) in the amisulpride and 16.7% (3 of 18) in the risperidone group. With regard to specific reasons, in each group 1 discontinuation occurred due to treatment failure. In addition, in the risperidone group, one patient had discontinuation due to adverse event and one was lost to follow-up. A total of 47.4% (9 of 19) and 50% (9 of 18) of the patients had adverse event during the trial. A total of 3 SAEs including 1 hospitalization for anxiety in the amisulpride as well as 1 sudden cardiac death and 1 hospitalization in the risperidone group. Neither of the two treatments was associated with statistically or clinically significant changes over time on measures of side effects including the total score on the Simpson Angus scale or the AIMS, respectively.
Date of report	24-Nov-2010