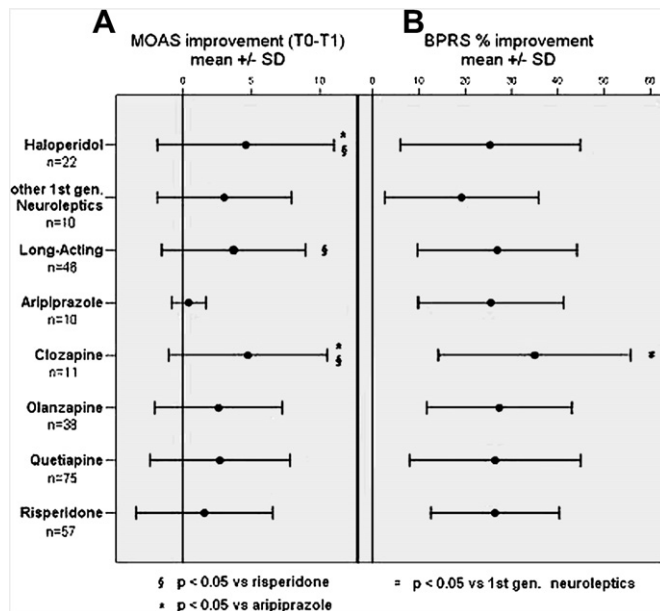


However, further researches are warranted to provide a better qualification of antipsychotic drugs on aggressive dimension



P0258

Placebo-controlled clinical trials of new atypical antipsychotics in schizophrenia

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Background: Placebo-controlled (PC) Phase 3 trials are critical for the registration of new atypical antipsychotic medications (AAP) for schizophrenia but use of placebo when efficacious treatments exist has been questioned.

Objective: To investigate evidence for the use of placebo in clinical trials of schizophrenia via a meta-analysis of large, PC trials of new AAPs.

METHODS: Using the FDA Summary Basis of Approval reports, we examined outcome data from all Phase 3 clinical trials that evaluated investigational AAPs. Publications from peer-reviewed literature were also identified. The main outcome variables were: symptom improvement in individual treatment arms, clinical response, therapeutic failure.

Results: Meta-regression indicated a highly significant difference between improvement in the placebo and the active arm ($p < 0.0001$). Effect size (ES) estimate for the placebo arm revealed that patients in this arm obtained a statistically significant but clinically negligible symptom reduction (Cohen d : ~ 0.15 ; $p < 0.004$) while active-treated patients displayed a substantial symptom reduction (Cohen d : ~ 0.70 ; $p < 0.0001$). Active treatments showed a highly significant ($p < 0.001$) superiority vs. placebo in clinical response and therapeutic failure, with failure rates often exceeding the rate of clinical response. ESs for change varied substantially across trials, with an ES range of $d = 0.8$ for the placebo and the active arms, respectively.

Conclusion: Variable ESs across studies support the view that placebo control has major importance in trials of new AAPs. However, efforts should focus on finding design alternatives and to minimize

the risks of PC trials so that they may be conducted in ethically acceptable manner.

P0259

Antipsychotics in psychiatric inpatients: Naturalistic data on first vs. repeated episodes

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Antipsychotics are widely used in psychiatric patients for various indications, beside psychosis most often in mood disorders, BPSD in dementia and agitation. Official guidelines are based on RCT data which differ from naturalistic data on the use of antipsychotics in real-life clinical setting.

The aim of our cross-sectional naturalistic study of hospitalized psychiatric patients ($n = 310$) was to get insight into prescription patterns for antipsychotics. We were especially interested in the class of antipsychotic, dose and combinations with other antipsychotics and other psychiatric drugs compared with diagnosis and number of hospitalizations. Structured data sheet was used to record data from medical records.

Results have confirmed the use of antipsychotics in variety of indications outside psychosis, especially mood disorders and agitation. Newer antipsychotics predominate although older antipsychotics have been used consistently in patients with longer illness duration and more hospitalizations (especially depot formulations), in acute agitation control as well as in acute mania and in combinations with atypical antipsychotics. Patients with first few hospitalizations are likely to receive antipsychotic therapy according to guidelines with atypical drugs in monotherapy. Equivalent doses for atypical antipsychotics although are usually higher than for typicals and lower for first hospitalizations.

The real-life use of antipsychotics is an important issue for different reasons including long-term treatment, burden of potential serious long-term side-effects as well as the quality of life in patients. Our data show that real-life uses of antipsychotics differ in some patient populations from recommended for various reasons that will be discussed.

P0260

Hospitalizations and compliance among schizophrenic patients in treatment with clozapine

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Objectives: Demonstrate that clozapine decrease the number of hospitalizations, and improve the adherence to treatment.

The sample consisted of 36 schizophrenia patients who were in treatment with a typical and atypical neuroleptic and then had their medication changed to clozapine. We ascertained the number of inpatient hospitalizations before starting clozapine and compared this with the number of hospitalizations after starting clozapine. We also followed an age- and gender-matched comparison group of other schizophrenia patients who were at treatment approximately the same time. Results indicate that the mean number of rehospitalizations while on other neuroleptic was bigger than after the commencement of clozapine treatment. The decrease in hospitalization rate for the comparison group was also statistically significant. The pre-post change was much greater for the clozapine patients than comparison

patients. A 2 x 2 repeated measures analysis of variance (ANOVA) contrasting the comparison group to the clozapine patients both before and after the index date indicates a significant time by group interaction, thus documenting the greater relative decrease in rehospitalization rate in the clozapine group.

We also used a compliance scale pre and post-beginning of treatment with clozapine for evaluate the adherence to treatment. Clozapine improve the compliance of treatment, in comparison to the neuroleptics that patient has taken before.

Conclusions: the clozapine seems to be more effective than other antipsychotics in decrease the risk of hospitalizations, and improve the adherence to treatment

P0261

Comparative mortality associated with ziprasidone vs. olanzapine in real-world use: The ziprasidone observational study of cardiac outcomes (zodiac)

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Background: Whether the modest QTc-prolonging effect of ziprasidone increases cardiovascular event risk is unknown.

Methods: The Ziprasidone Observational Study of Cardiac Outcomes (ZODIAC), an open-label, randomized, postmarketing study, enrolled patients with schizophrenia from routine clinical practice settings in 18 countries. The primary outcome was non-suicide mortality in the year after initiation of assigned treatment. A total of 18,154 subjects were randomized to ziprasidone or olanzapine, dosed according to enrolling physician's clinical judgment. A physician-administered baseline questionnaire collected information on demographics, medical and psychiatric history, and concomitant medication use. Brief follow-up questionnaires elicited hospitalization data since the last study visit, vital status, study medication continuation, and concomitant antipsychotic medication(s) use. ZODIAC study subjects reflected the general population of patients with schizophrenia.

Results: The incidence of nonsuicide mortality within one year of initiating therapy was 0.91% for the ziprasidone group and 0.90% for the olanzapine group (both n = 9,077), relative risk (95% confidence interval [CI]) of 1.01 (0.75, 1.37). This finding was robust in numerous secondary and sensitivity analyses. Regarding secondary endpoints, the risk of all-cause mortality or cardiovascular mortality was similar among ziprasidone and olanzapine users; the incidence of all-cause hospitalizations was higher among ziprasidone users. The proportion of patients remaining on treatment at 6 months was lower for the ziprasidone group.

Conclusions: ZODIAC is one of the largest randomized studies conducted to date of patients with schizophrenia. With substantial statistical power, the study found no difference in risk of nonsuicide death associated with the use of ziprasidone vs. olanzapine.

P0262

Risperidone and liver function tests in children and adolescents: A short term prospective study

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Objective: Revealing of unknown adverse effects of atypical antipsychotics on pediatric population may take a long period of time. The purpose of this prospective study is to document changes in the liver function tests (LFTs) associated with Risperidone usage in a group of children and adolescents.

Method: Study subjects consist of 120 youths with ages ranging from 3-17 years. For this study, patients' baseline and follow-up weight and liver function tests (LFT) including alanine aminotransferases (ALT) and aspartat aminotransferases (AST), gamma glutamyl transesterase (GGT), alkaline phosphatase (ALP) and serum bilirubin levels were measured before and after the treatment period of one month.

Results: Only one eight years old male patient's ALT levels increased up to three-fold and AST levels increased up to two-fold of the basal levels. First month mean levels of liver enzymes and bilirubin of the patients were significantly higher than the baseline. One or more of the liver enzymes and/or bilirubin levels of sixty-three patients (52.5%) showed an asymptomatic increase in the first month of this study. Weight gain was observed in 58 patients (57.4%). There was no significant association between changes in weight and liver enzymes and bilirubin levels.

Conclusion: We found asymptomatic LFT abnormalities mostly in the form of ALP elevation in 52.5% and marked liver enzymes elevation in 0.8% of risperidone treated subjects. These findings suggest that risperidone treatment in the short term commonly leads to liver function changes however it rarely may induce a serious hepatic toxicity at therapeutic doses in children and adolescents.

P0263

Effect of risperidone long-acting injection on hospitalisation: A mirror image analysis

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The aim of this study was to assess the effect of risperidone long-acting injection (RLAI) on hospitalisation using a mirror image analysis.

Data on the number of admissions and number of days in hospital were analysed during the two-year period before starting RLAI and the duration of therapy in 56 patients.

Admission rates and length of hospitalisation both decreased for approximately 60% of patients during RLAI therapy.

The time in hospital was significantly lower (p=0.002) during RLAI therapy compared to the previous two years. During the pre-