from baseline <1 msec); risperidone increased QTc interval by approximately 6 msec. Aripiprazole is effective in the treatment of positive and negative symptoms. Its safety and tolerability profile may offer short- and long-term treatment benefits.

P02.16
Increased rates of antipsychotic-induced eps in mania: myth or reality

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The purpose of this study is to determine antipsychotic-induced extrapyramidal symptom (EPS) vulnerability in bipolar disorder compared to schizophrenia. Acute EPS profiles of patients with bipolar disorder were compared from randomized double-blind trials of olanzapine (5–20 mg/d, n=125) versus placebo (n=129) and olanzapine (5–20 mg/d, n=234) versus haloperidol (3–15 mg/d, n=219). Findings were compared to those from olanzapine-placebo and olanzapine-haloperidol trials in schizophrenia. EPS was assessed as: 1) unsolicited extrapyramidal adverse events; 2) objective rating scales; and 3) concomitant use of anticholinergics. Olanzapine was not significantly different from placebo on any of these EPS assessments yet was compared to haloperidol. These analyses were compared with findings in placebo- and haloperidol-controlled olanzapine studies for schizophrenia. While placebo and olanzapine groups exhibited EPS profiles similar to like-treated patients with schizophrenia, the haloperidol group exhibited more severe profiles than like-treated patients with schizophrenia. These findings support the observation of increased EPS vulnerability in bipolar patients treated with conventional antipsychotics. This however does not appear to be the case for olanzapine, which had placebo-like rate of EPS across schizophrenia and bipolar disorders.

P02.17
Controlled study of aripiprazole and haloperidol in schizophrenia

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This double-blind, 4-week study compared the efficacy and safety of aripiprazole, a dopamine-serotonin stabilizer, with haloperidol and placebo in 414 hospitalized patients with acute relapse of schizophrenia or schizoaffective disorder randomized to aripiprazole (15 mg or 30 mg daily), haloperidol (10 mg/day), or placebo. Efficacy measures included PANSS and CGI. Both doses of aripiprazole and haloperidol were significantly more effective than placebo (change in PANSS-total, BPRS-total, LOCF: $p<0.01$). Responder rates (¡Y30% decrease from baseline in PANSS-total at last visit) were significantly better for both aripiprazole doses than for placebo ($p<0.05$), but did not differ significantly between haloperidol and placebo. Fewer patients discontinued treatment due to adverse events with aripiprazole than with placebo or haloperidol. Aripiprazole-treated subjects showed no clinically meaningful increases in QTc prolongation, and had extrapyramidal symptoms comparable to subjects receiving placebo. With aripiprazole, the mean change in plasma prolactin levels was comparable to placebo and less than haloperidol, while the incidence of clinically significant weight gain was less than with haloperidol. This study demonstrates the clinical efficacy and tolerability of aripiprazole for treating schizophrenia and schizoaffective disorder.

P02.18
Ziprasidone vs amisulpride for negative symptoms of schizophrenia

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Objective: To compare efficacy of ziprasidone and amisulpride for negative symptoms and overall psychopathology in schizophrenia.

Method: This multicenter, double-blind trial enrolled patients with schizophrenia and a >6 points higher PANSS Negative than Positive subscale score. Patients were randomized to ziprasidone (40–80 mg BID; n=59) or amisulpride (50–100 mg BID; n=63) for 12 weeks. Efficacy evaluations (PANSS negative, PANSS total, GAF, BPRS, CGI-S, CGI-S) occurred at baseline and weeks 4, 8, and 12. Endpoints were equivalency ratios of mean changes from baseline, with equivalency established if the lower limit of the 95% CI of the ratio exceeded 0.60.

Results: For both treatment groups, the mean decrease in PANSS Negative Subscale scores over 12 weeks was significant and equivalent (no significant between-group differences from baseline to last visit). Improvements from baseline were also observed in PANSS Total, GCI-S and CGI-I, BPRS Total and Core, and GAF scores, with no significant differences between groups. Both treatments were generally well tolerated.

Conclusions: Ziprasidone demonstrates comparable efficacy to amisulpride in improving negative symptoms and global psychopathology of patients with schizophrenia.

P02.19
Aripiprazole: a dopamine-serotonin system stabilizer

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Aripiprazole is the first of the next generation of atypical antipsychotics which has demonstrated sustained antipsychotic efficacy with an excellent safety and tolerability profile. The binding affinity and functional activity of aripiprazole at dopamine and serotonin receptors have been investigated using CHO cells expressing human recombinant D2L receptors and 5HT1A receptors. Aripiprazole bound with high affinity to D2L receptors and potently activated D2L receptors coupled to the inhibition of cAMP accumulation with relative intrinsic activity less than that of dopamine. Aripiprazole bound with high affinity to 5HT1A receptors and stimulated basal [35S]GTPgammaS binding to 5-HT1A receptors by 68.1% relative to the maximal effect of serotonin. Buspirone displayed a similar level of relative intrinsic activity to that of aripiprazole. Aripiprazole also binds in a monophasic fashon to 5HT2A receptors and blocks 5HT-agonist-induced head twitches in mice, an effect consistent with 5-HT2A antagonism. Together these data suggest aripiprazole is a dopamine-serotonin system stabilizer and this profile may underlie aripiprazole's clinical benefits, including improvement of positive, negative, and affective symptoms with minimal risk for EPS and prolactin elevation.