

**Conclusions:** Ziprasidone and olanzapine yielded comparable improvement in psychopathology and global illness severity measures, but there were significant differences favoring ziprasidone in important general health parameters.

### P02.12

Recent weight gain and cost of acute service use in schizophrenia

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**Objective:** To consider the association between recent weight gain and acute service use in schizophrenia.

**Methods:** Questionnaires were mailed to people with schizophrenia identified through NAMI and NMHA (N=390). 345 respondents reported lost weight (n=94, 27%), no change (n=106, 31%), some gain (1¼V14 lb; n=70, 20%), and significant gain (>15 lb; n=75, 22%) in last 6 months. Acute service use was defined as emergency room (ER) visit or hospitalization. Cost was estimated conservatively at \$817/day for hospital days (average Medicare reimbursement), and at \$85 for ER visits.

**Results:** Patients with significant weight gain were significantly more likely to use acute services (P<0.001, hospitalization; P<0.005, ER), with significance evident even after multivariate analysis. Combined hospitalization/ER costs were highest for those who gained >15 lb (\$9,486), followed by those who lost weight (\$7,400), those without weight change (\$4,095), and those who gained 1¼V14 lb (\$3,647).

**Conclusions:** Significant weight gain is associated with greater use of acute services and higher costs in schizophrenia. If weight gain is due to use of certain newer antipsychotics, it may lead to medication noncompliance.

### P02.13

Application of rispolept at heroin addiction in outpatient practice

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**Objectives:** research of efficiency of neuroleptic – rispolept for the prevention of development and reduction of compulsive craving for to heroin at patients in postwithdrawal period.

**Method:** it is observed 30 patients with heroin addiction. Age of patients was from 18 till 39 years, duration of disease from 1 till 5 years. Clinical-psychopathological and statistical methods of research were used.

**Results:** after the reduction of acute withdrawal syndrome at patients the unstable condition when the craving for heroin is easily actualized is observed. Quite often it is manifested by psychopathological disorders. In this connection patients require in prolong (sometimes about half-year and more) application of neuroleptics with the least by-effects. Rispolept was used to patients from 7–14 days after the last reception of a heroin, in a doze 4–6 mg per day (on 2–3mg in the morning and to night). In a day after application of rispolept the patients marked the improvement of mood, reduction of affective intensity and malice. After the discharge from a hospital, in 3–4 weeks rispolept was used in out-patient practice and, as a rule, in previous dosages. At patients stabilization of an emotional background, dysphoric reactions, psychopathological behavior, compulsive craving for heroin were marked. At the same time the extrapyramidal semiology was observed extremely seldom and was insignificantly expressed. Application of rispolept did not require the combined therapy with other neuroleptics, and also proofs. At increasing of depression the antidepressants were used.

The prolong application of rispolept including the remission period, reduced a level of affective instability, asthenia, divergences. At patients interest to environmental conditions and life was restored, communicative functions were improved.

**Conclusion:** the results of research testify to perspectivity of practical application of atypical neuroleptic rispolept, as safe normothymic, as supporting and antirecurrent treatment in out-patient practice of heroin addiction.

### P02.14

Patient attitude after switch to ziprasidone from other antipsychotics

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**Objective:** To determine change in patient attitudes/feelings about drug therapy after switching from other antipsychotics to ziprasidone.

**Method:** Three 6-week multicenter, open-label, parallel-group trials in stable outpatients with schizophrenia who were switched from conventional antipsychotics (n=108), olanzapine (n=104), or risperidone (n=58) to ziprasidone (40–160 mg/day). Patients were randomized to 1 of 3 strategies. A 10-question Drug Attitude Inventory (DAI) was administered at baseline and week 6. Positive total score indicated likely compliance; negative total score, likely noncompliance. Marginal probabilities of favorable responses over total, attitudinal, and subjective question sets were assessed.

**Results:** Total DAI scores improved significantly in patients switched to ziprasidone from conventionals (P=0.003) or risperidone (P=0.008). Categorical analysis identified significant improvements in patients switched to ziprasidone from conventionals (P=0.05 all items, P=0.02 subjective) and a trend toward improved scores after switching from olanzapine (P=0.06 for both). DAI improvement was driven by positive change in subjective feelings. Ziprasidone was well-tolerated and effective, regardless of dose or switch strategy.

**Conclusions:** Outpatients with schizophrenia report better subjective feelings about medication use after switching to ziprasidone.

### P02.15

Aripiprazole and risperidone versus placebo in schizophrenia

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This multicenter, double-blind, controlled study examined the efficacy, safety, and tolerability of aripiprazole, the first of the next generation of atypical antipsychotics in patients with acute relapse of schizophrenia or schizoaffective disorder randomized to aripiprazole 20 mg qd (n=101) or 30 mg qd (n=101), risperidone 3 mg bid (n=99), or placebo (n=103) for 4 weeks. Efficacy evaluations included PANSS and CGI. At week 4, both aripiprazole doses and risperidone were significantly better than placebo on all efficacy measures (p<0.05). Aripiprazole separated from placebo for all PANSS scores by week 1, as did risperidone (except PANSS-negative score [week 2]). No significant EPS were observed with active treatment versus placebo. Active treatments were associated with minimal weight gain. Mean prolactin level showed no significant change from baseline with aripiprazole, but increased 5-fold with risperidone (p<0.001). Aripiprazole was not associated with clinically significant QTc interval prolongation (mean change

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 (≥30% 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-I) 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, CGI-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 fashion 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.