Switching to Olanzapine From Previous Antipsychotics: A Regional Collaborative Multicenter Trial Assessing 2 Switching Techniques in Asia Pacific

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Background: This open-label, multicenter, randomized study compared the efficacy and safety of switching moderately ill Asian patients with schizophrenia from their current regimen of antipsychotic medication to the atypical antipsychotic olanzapine using either a direct switch method or a start-taper switch method.

Method: Asian inpatients and outpatients with DSM-IV schizophrenia (N = 108) currently treated with predominantly typical antipsychotics were switched to olanzapine (initial dose of 10 mg/day) for 6 weeks. Patients were randomly assigned to 1 of 2 groups: the direct switch group (N = 54) received only olanzapine, while the start-taper switch group (N = 54) received olanzapine and their usual antipsychotic in decreasing doses for the first 2 weeks. A successful switch was defined as completing 6 weeks of therapy without worsening of symptoms (Clinical Global Impressions-Severity of Illness scale [CGI-S]) or extrapyramidal side effects (Simpson-Angus Scale). Overall efficacy was assessed using the Positive and Negative Syndrome Scale (PANSS), and safety was assessed by recording adverse events and measuring vital signs.

Results: Statistically significant ($p < .001$) improvements from baseline to endpoint occurred in both switch groups in the CGI-S score and the PANSS total score and subscores. However, no significant differences were observed between the switch groups for any efficacy measure. Both techniques had comparable rates of successful switching (direct switch, 74.1% vs. start-taper switch, 67.9%). The frequency of treatment-emergent adverse events was similar between switch groups with no clinically significant differences in any laboratory value or vital sign. Weight gain occurred in both switch groups ($p < .001$), but the groups were not statistically different from each other. Both switch groups showed statistically significant ($p < .01$) improvements from baseline to endpoint on the Simpson-Angus Scale and Barnes Akathisia Scale.

Conclusion: Moderately ill Asian patients with schizophrenia may experience a decrease in symptom severity and improvement in extrapyramidal symptoms when switched from their current medication to olanzapine therapy.

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The conventional, or typical, antipsychotics, such as haloperidol and chlorpromazine, are the most commonly used medications for treating schizophrenic patients in Asian populations. However, these drugs have several important limitations. Even though the typical antipsychotics are quite effective in treating the positive symptoms of schizophrenia, they have little effect on negative symptoms, mood disturbances, cognitive dysfunctions, and anxiety. It is estimated that 70% of patients on treatment with typical antipsychotics experience a suboptimal response and another 15% show little or no response.[1] Up to 70% of these patients may relapse after initial improvement during maintenance therapy.[2–4]

The incidence of acute extrapyramidal symptoms (EPS) may be as high as 40% in patients receiving typical antipsychotics.[5] Several studies have shown that Asian patients are more susceptible to developing EPS even after taking low doses of haloperidol.[6,7] The incidence rate of developing tardive dyskinesia (TD) in patients treated with typical antipsychotics is 5% per year of exposure[8,9] with a 20% to 50% likelihood of a patient acquiring TD on long-term typical antipsychotic therapy.[10,11] In addition, there is evidence that patients with drug-induced EPS may have a greater risk of developing TD,[12,13] which makes the need for treatment alternatives to typical antipsychotics in Asian populations even more critical. Importantly, increased rates of EPS and TD may contribute

to noncompliance, which increases the chance for relapse and long-term disability.[14,15]

The atypical antipsychotic olanzapine may be a treatment option for patients who need to switch from their present medication. Olanzapine has demonstrated improved efficacy compared with haloperidol for negative symptoms and at least equivalent efficacy for positive symptoms of schizophrenia.[16–18] Previous studies have shown that olanzapine-treated patients have a low propensity for experiencing EPS[17,19] and TD[20,21] and that olanzapine may actually be used as a treatment for alleviating TD symptoms.[20,22–24] Olanzapine should be an effective alternative therapy, but few studies have characterized the efficacy and safety of olanzapine in Asian patients.[25]

The primary objective of this study was to determine whether moderately ill Asian schizophrenic patients could be switched from their previous medication to olanzapine with minimal adverse clinical consequences and whether there was any advantage in a start-taper switch technique over a direct switch. We also wanted to determine whether patients who were switched to olanzapine benefited from an improvement in severity of symptoms or preexisting EPS. This study was conducted as an uncontrolled, randomized, open-label, multicenter study to imitate the normal treatment conditions of the clinical setting in Asian countries.

METHOD

Patient Population

In this multicenter, open-label, randomized, parallel study, 120 patients were screened in Australia, Hong Kong, Malaysia, the Philippines, Singapore, Taiwan, and Thailand. For patients to be included in the study, they had to be at least 18 years old, of Asian origin, and meet DSM-IV criteria for schizophrenia. They could be inpatients or outpatients of either sex. Patients were required to receive their usual antipsychotic medication for a minimum of 4 weeks prior to entering the study. The institutional or ethical review board at each study site approved the study protocol, and written informed consent was obtained from each patient after the study was described in detail.

Study Design

Study period 1 was a 1-week screening period. Visit 1 consisted of administering screening tests, conducting psychiatric and physical examinations, and gathering patient histories, although duration of illness, number of previous episodes, and length of drug treatment were not captured. Patients were allowed to continue their usual antipsychotic treatment during the first week. If a patient was on treatment with more than 1 antipsychotic, all but 1 antipsychotic was discontinued at visit 1. Patients with a history of a serious, unstable illness, 1 or more seizures with unknown etiology, or DSM-IV substance dependence within the past 2 months were excluded. Patients who were currently treated with clozapine or had been treated with a depot antipsychotic less than 4 weeks prior to visit 1 were also excluded. Study period 2 consisted of 6 weeks of open-label therapy. If patients met all enrollment criteria at visit 2, they were randomly allocated (1:1) to either the direct switch or start-taper switch group. Patients randomly assigned to the direct switch group immediately discontinued their current antipsychotic medication and initiated olanzapine therapy at 10 mg/day. After visit 2, the olanzapine dosage could be adjusted within the allowed dose range of 5 to 20 mg/day. Patients randomly assigned to the start-taper group received olanzapine (10 mg/day) in addition to their current antipsychotic at decreasing doses over the next 2 weeks. In this group, the olanzapine dosage could also be adjusted in the range of 5 to 20 mg/day. A single benzodiazepine was permitted daily during the study; however, a patient would be discontinued if he or she required multiple types of benzodiazepines. For treating acute EPS, anticholinergics could be given in doses up to 4 mg/day of benztropine equivalent but not exceeding 2 days per week. The use of anticholinergic medication as prophylaxis for EPS was prohibited.

Assessments

The safety profile of switching to olanzapine was assessed by the collection of treatment-emergent adverse events during the open-label treatment phase. Akathisia and EPS were assessed using the Barnes Akathisia Scale[26] and Simpson-Angus Scale,[27] respectively. Laboratory analyses (clinical chemistry, electrolytes, and hematology) were measured at visit 1 and when a patient completed or discontinued the study or when clinically indicated. Vital signs (blood pressure, heart rate, weight, and temperature) were measured at every visit.

The efficacy of olanzapine was measured using the Positive and Negative Syndrome Scale (PANSS)[28] total and subscores (positive, negative, and general psychopathology) and the Clinical Global Impressions-Severity of Illness scale (CGI-S).[29] Response on efficacy measures was defined a priori as 20% or more improvement in the PANSS total score from baseline to endpoint.

The primary objective of this study was to determine if a successful switch was made from a patient's previous antipsychotic to olanzapine. A successful switch was defined as the completion of 6 weeks of therapy without worsening of symptoms (2 successively worse ratings from baseline on the CGI-S) and without exacerbation of EPS (an increase from baseline Simpson-Angus Scale values in any postbaseline visit).

Statistical Analyses

All statistical analyses were performed on an intent-to-treat basis, and all endpoint analyses employed a last-

Table 1. Patient Demographic and Baseline Illness Characteristics[a]

Variable	Direct (N = 54)	Start-Taper (N = 54)	Total (N = 108)	Overall p Value
Sex, N (%)				
Male	24 (44.4)	30 (55.6)	54 (50.0)	.248
Female	30 (55.6)	24 (44.4)	54 (50.0)	
Age, mean ± SD, y	34.5 ± 9.9	37.1 ± 11.1	35.8 ± 10.54	.221
PANSS score, mean ± SD				
Total	80.4 ± 27.0	75.0 ± 23.9	77.7 ± 25.5	.385
Positive	18.5 ± 6.7	17.1 ± 6.1	17.8 ± 6.4	.311
Negative	22.0 ± 10.1	21.5 ± 8.6	21.8 ± 9.3	.844
General psychopathology	39.8 ± 13.2	36.4 ± 12.4	38.1 ± 12.8	.264
CGI-S score, mean ± SD	4.2 ± 1.2	3.9 ± 1.0	4.0 ± 1.1	.417
Length of current treatment, mean ± SD, wk	146.9 ± 204.4	171.3 ± 249.6	158.6 ± 226.1	.589

[a]Abbreviations: CGI-S = Clinical Global Impressions-Severity of Illness scale, PANSS = Positive and Negative Syndrome Scale.

observation-carried-forward (LOCF) method. To be included in analyses of change from baseline to endpoint, patients must have had both a baseline score (visit 2, unless missing, then visit 1) and at least 1 postbaseline score. The Pearson chi-square test was used for analyzing proportions such as switching success, patient disposition, and sex ratio. Baseline-to-endpoint changes and within-group analyses were evaluated with the paired t test. For continuous efficacy and safety parameters, analysis of variance (ANOVA) was used to compare treatment effects between the 2 switching groups; the model included the terms of treatment, country, and treatment-by-country interaction. Treatment-by-country interaction was tested at an α level of .10. Visitwise analyses were performed using an ANOVA on observed cases (OC) at each timepoint; the model included the terms of treatment and country. Treatment-emergent adverse events were defined as events that first occurred or worsened after baseline, and frequencies were compared using the Fisher exact test. For all analyses, treatment effects were tested at the 2-sided α level of .05.

RESULTS

Patient Demographics

From the initial 120 patients screened at baseline, a total of 108 patients were randomly assigned to a switching group. All patients were of Asian origin (east or southeast Asian ethnic groups), and 50% were male. The mean ± SD age of patients in this study was 35.8 ± 10.5 years (range, 18–62 years). There were no significant differences in age, sex, PANSS scores, CGI-S scores, or length of current treatment between the 2 switch groups (Table 1). There were also no significant differences between the switch groups in the type of antipsychotic medications used previously. In the direct switch group, 51 patients (94.4%) were taking at least 1 typical antipsychotic and 10 (18.5%) were taking at least 1 atypical antipsychotic; in the start-taper switch group, 46 (85.2%) were taking at least 1 typical antipsychotic and 13 (24.1%) were taking at least 1 atypical antipsychotic. Haloperidol was the most commonly prescribed antipsychotic for both the direct switch group (38.9%) and the start-taper switch group (40.7%).

Table 2. Patient Disposition

Reason for Discontinuation	Direct (N = 54) N	%	Start-Taper (N = 54) N	%	Total (N = 108) N	%	p Value
Protocol complete	45	83.3	47	87.0	92	85.2	.588
Adverse event	1	1.9	1	1.9	2	1.9	> .999
Lost to follow-up	3	5.6	1	1.9	4	3.7	.308
Patient decision	1	1.9	0	0.0	1	0.9	.315
Criteria not met	1	1.9	3	5.6	4	3.7	.308
Physician decision	3	5.6	2	3.7	5	4.6	.647

Patient Disposition

Of the original 108 patients, 92 (85.2%) completed the study. Forty-five patients (83.3%) in the direct switch group finished the study compared with 47 patients (87.0%) in the start-taper switch group (p = .588) (Table 2). No statistically significant differences were found between switch groups in any reason for discontinuation.

Dosage

The mean modal daily doses of olanzapine were 12.6 ± 4.2 mg/day for the direct switch group and 11.7 ± 3.5 mg/day for the start-taper switch group. The mean daily doses of olanzapine were 12.2 ± 3.2 mg/day for the direct switch group and 11.5 ± 2.6 mg/day for the start-taper switch group.

Concomitant Medications

During the open-label olanzapine treatment phase, 37 patients (68.5%) in the direct switch group were taking at least 1 other type of non-neuroleptic medication compared with 43 (79.6%) in the start-taper switch group. Specifically, 22 patients (40.7%) in both the direct and start-taper switch groups received at least 1 dose of a benzodiazepine during the open-label phase. Thirteen patients (24.1%) in the direct switch group and 17 patients (31.5%) in the start-taper switch group took at least 1 dose of an anticholinergic drug during the open-label phase. No between-group differences in use of concomitant medications were statistically significant.

Efficacy

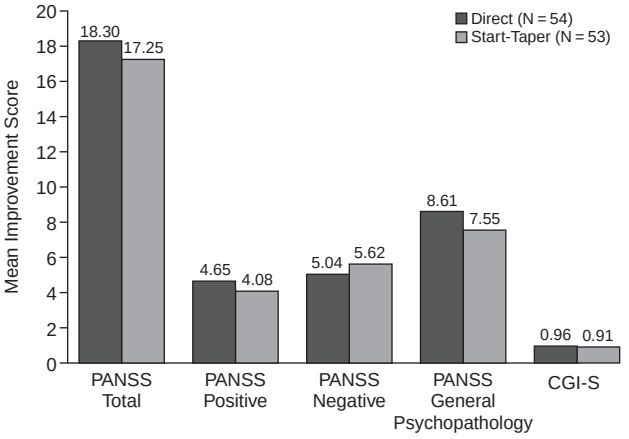
On the primary efficacy measure (CGI-S), the percentage of patients successfully switching in the direct switch

group was 74.1% (40/54) compared with 67.9% (36/53; 1 patient had no postbaseline measurement) in the start-taper switch group. There was no statistically significant difference in the percentages of successfully treated patients between switch groups (p = .483). In addition, the 95% confidence interval for the difference in success rates (direct minus start-taper) included 0, suggesting no statistically significant difference (–11.01% to 23.1%).

The changes from baseline to endpoint for the CGI-S and the PANSS total score and subscores are shown in Figure 1. There were no significant differences in any efficacy scale between switch groups for LOCF mean change from baseline. However, patients in both switch groups experienced a statistically significant mean improvement from baseline on all of these efficacy measures (p < .001). Scores for both switch groups improved by at least 20% (20.6%–25.9%) on each efficacy measure.

The OC visitwise change from baseline is shown in Figures 2A through 2E. Patients in both switch groups were significantly improved (p < .001) compared with baseline at all timepoints (weeks 1, 2, 4, and 6) for the PANSS total, positive, and general psychopathology scores. The switch groups were also significantly improved from baseline at all timepoints on the PANSS negative (p = .01) and CGI-S (p < .05) measures. No statistically significant differences occurred between switch groups at any timepoint for any of the efficacy measures except for a statistically significant interaction (switch-group-by-country, p = .064) for the PANSS negative score at week 1.

Figure 1. Mean Endpoint Improvement in Efficacy Scores (last observation carried forward)[a]



[a]p < .001 for all within-group comparisons for all efficacy scales. There were no statistically significant differences between switch groups for any efficacy scale. Abbreviations: CGI-S = Clinical Global Impressions-Severity of Illness scale, PANSS = Positive and Negative Syndrome Scale.

Safety

The frequency of treatment-emergent adverse events (≥ 5% of patients) for both switch groups is shown in Table 3. The most commonly reported treatment-emergent adverse events among direct switch patients were somnolence, insomnia, and headache (all 11.1%). Among start-taper switch patients, the most common events were somnolence (14.8%), headache (9.3%), and insomnia and increased appetite (both 7.4%). One patient in each switch group discontinued because of somnolence. No serious adverse events occurred in either switch group, and there was no statistically significant difference between switch groups for any adverse event.

None of the changes in laboratory values from baseline to endpoint were considered clinically significant, and no statistically significant differences occurred between switch groups in any laboratory value.

There was a statistically significant (p < .001) weight gain from baseline during the open-label phase for patients in both the direct switch (1.93 ± 2.72 kg [4.28 ± 6.04 lb]) and start-taper switch (1.29 ± 2.77 kg [2.86 ± 6.15 lb]) groups; however, the weight gain was not statistically different between the 2 groups (p = .065). Several statistically significant changes in pulse and blood pressure were observed in both groups, but these changes were considered clinically insignificant.

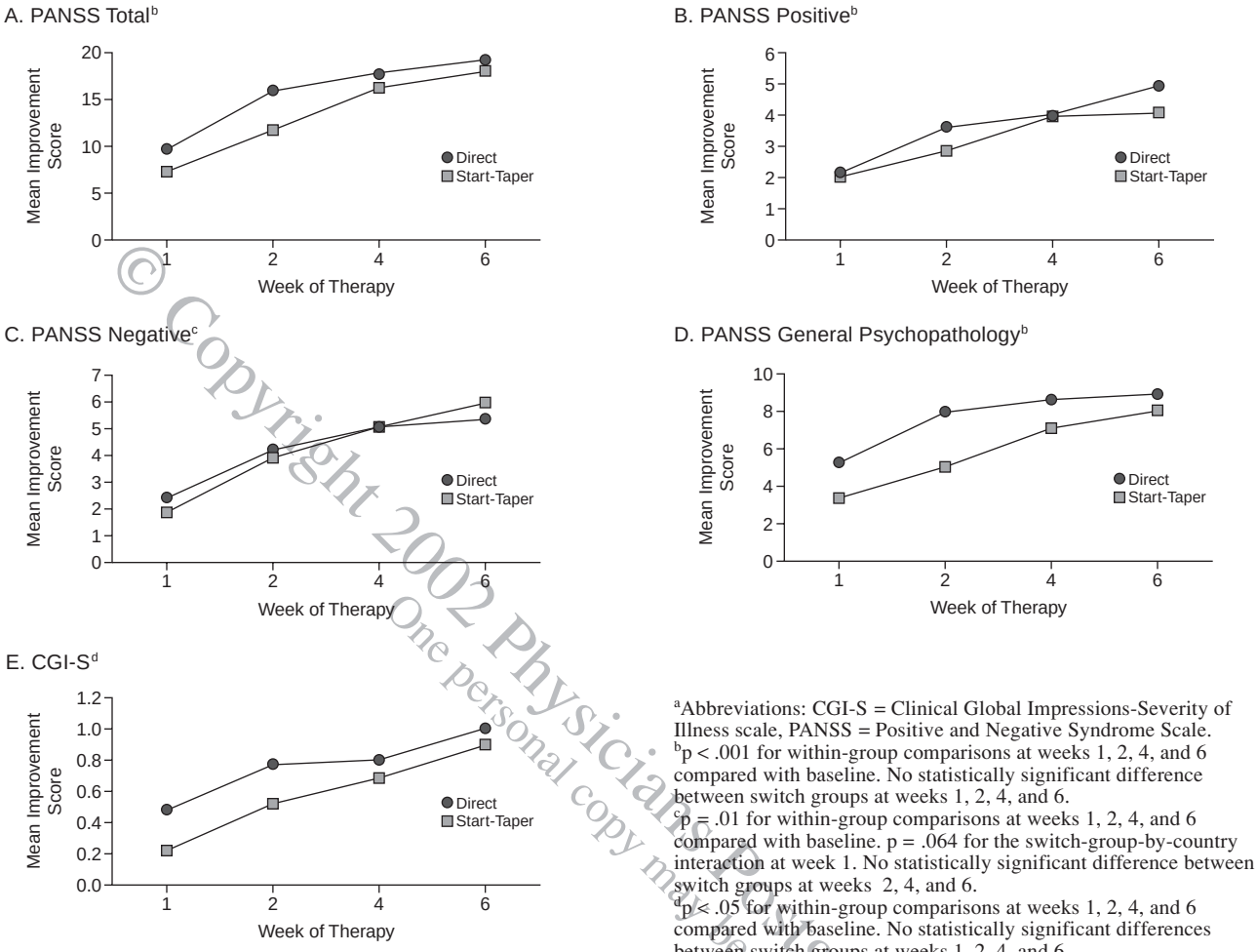
Patients in both groups showed statistically significant improvements (p < .01) from baseline in Simpson-Angus Scale and Barnes Akathisia Scale scores during the open-label phase (Figure 3). No significant difference was found between the switch groups for either score.

DISCUSSION

More than two thirds of the patients in each group were successfully switched to olanzapine from another antipsychotic. Patients in both groups improved significantly from baseline on all efficacy and EPS measures, but there were no significant differences between the groups for any of these measurements. Less than 2% of patients discontinued the study because of treatment-emergent adverse events. There were no serious adverse events in either switch group, and no clinically significant changes occurred for any laboratory value or vital sign. Weight gain did occur in both groups, but no patient discontinued for that reason. This is the first large multinational trial of an atypical antipsychotic in Asia and the first study to compare switching to olanzapine from other antipsychotics, as well as comparing switching techniques, in Asian schizophrenic patients.

Our study demonstrated that olanzapine was effective in significantly reducing both symptomatology and EPS in the majority of patients. Importantly, symptom control is the primary objective for switching patients to a different antipsychotic. This is especially true for many patients on treatment with typical antipsychotics because these

Figure 2. Visitwise Change From Baseline on the PANSS and CGI-S (observed cases)[a]



[a]Abbreviations: CGI-S = Clinical Global Impressions-Severity of Illness scale, PANSS = Positive and Negative Syndrome Scale.
[b]$p < .001$ for within-group comparisons at weeks 1, 2, 4, and 6 compared with baseline. No statistically significant difference between switch groups at weeks 1, 2, 4, and 6.
[c]$p = .01$ for within-group comparisons at weeks 1, 2, 4, and 6 compared with baseline. $p = .064$ for the switch-group-by-country interaction at week 1. No statistically significant difference between switch groups at weeks 2, 4, and 6.
[d]$p < .05$ for within-group comparisons at weeks 1, 2, 4, and 6 compared with baseline. No statistically significant differences between switch groups at weeks 1, 2, 4, and 6.

drugs have little effect on depression, cognition, and anxiety. Patients who are moderately ill will continue to have a difficult time trying to reenter society, much less the workforce. Moreover, many of these patients will lack appropriate insight and may become noncompliant and relapse. Patients who do gain symptom control on treatment with typical antipsychotics often experience sexual dysfunction, EPS, and TD.[30] Many patients will stop taking their medication because of these side effects and will relapse. According to the Expert Consensus Guidelines for treating schizophrenia,[31] patients should be switched from typical antipsychotics to atypical antipsychotics if they have persistent positive or negative symptoms, EPS, risk of TD, or other disturbing side effects.

In contrast, patients on treatment with atypical antipsychotics have shown only a very small risk for EPS, TD, and sexual dysfunction. In particular, switching to olanzapine has been shown to be beneficial not only in mildly to moderately ill schizophrenic populations[32] but also in markedly to severely ill patients.[33] Therefore, schizophrenic patients who are mildly to severely ill and those who have EPS, TD, or sexual dysfunction while on their current treatment are candidates for being switched to olanzapine or another atypical antipsychotic.

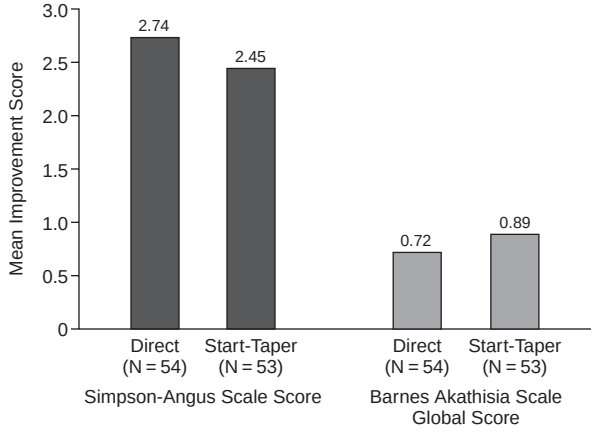
The efficacy results we found were remarkable considering that the patient population had been treated with antipsychotics for at least 4 weeks before entering our study. It is likely that many patients had been treated with more than 1 antipsychotic and for a much longer period. In addition, the patient population was moderately ill, yet still improved significantly on all efficacy measures. Patients with severe symptoms[33] and who were treatment refractory[33–35] have also been successfully switched to olanzapine.

The patients in this study also showed significant improvement in EPS and akathisia. In contrast, Asian patients treated with haloperidol have been shown to be more susceptible to EPS than white patients with schizophrenia even after lowering their dosage.[6,7] In support of both of these findings, a recent study found that EPS and

Table 3. Treatment-Emergent Adverse Events Reported by ≥ 5% of Patients in Either Switch Group

	Direct (N = 54)		Start-Taper (N = 54)		Total (N = 108)		
Adverse Event	N	%	N	%	N	%	p Value
Somnolence	6	11.1	8	14.8	14	13.0	.776
Headache	6	11.1	5	9.3	11	10.2	> .999
Insomnia	6	11.1	4	7.4	10	9.3	.742
Akathisia	5	9.3	3	5.6	8	7.4	.716
Increased appetite	4	7.4	4	7.4	8	7.4	> .999
Asthenia	4	7.4	2	3.7	6	5.6	.678
Agitation	3	5.6	1	1.9	4	3.7	.618
Weight gain	3	5.6	0	0.0	3	2.8	.243
Tremor	2	3.7	3	5.6	5	4.6	> .999
Diarrhea	0	0.0	3	5.6	3	2.8	.243

Figure 3. Mean Endpoint Improvement in Extrapyramidal Scores (last observation carried forward)[a]



[a]p < .01 for within-group comparisons compared with baseline for each scale. There was no statistically significant difference between switch groups.

akathisia were improved in Japanese schizophrenic patients treated with olanzapine but worsened in patients treated with haloperidol.[25] In another recent study, a high percentage of Hispanic patients (also more susceptible to EPS than white individuals) with haloperidol-induced EPS showed significant improvement 6 weeks after directly switching to olanzapine.[36] Finally, some recent trials have shown improvements in safety measures with olanzapine compared with haloperidol in patients of Chinese descent.[23] Therefore, the results from the present and previous studies suggest that patients can be safely switched to olanzapine from previous antipsychotics and actually improve their existing EPS.

An important consideration, especially in Asian populations, is the possible development of TD from treatment with the typical antipsychotics. Several studies have shown that patients with EPS have a statistically significantly greater chance of developing TD compared with patients without a history of EPS.[12,13] As shown above, patients treated with olanzapine have a low propensity for developing EPS. A recent meta-analysis of 4 large clinical trials comparing olanzapine with haloperidol and placebo showed no significant difference in the Barnes Akathisia Scale and Simpson-Angus Scale scores for olanzapine compared with placebo, whereas haloperidol had significantly higher scores compared with placebo.[16] In addition, 2 studies have shown that the incidence of TD was much lower with olanzapine treatment compared with haloperidol in patients on long-term treatment with these antipsychotics.[20,21] A lower incidence of EPS and TD has also been demonstrated with other atypical antipsychotics.[37] Accordingly, the expectation is that Asian patients treated with olanzapine or other atypical antipsychotics should develop TD at significantly lower rates than patients on treatment with typical antipsychotics.

Patients in both switch groups gained a mean of less than 2 kg over the 6-week study. A recent study found that Japanese schizophrenic patients treated with olanzapine for 8 weeks gained a mean of less than 1 kg.[25] These weight gains are less than those typically found in studies consisting primarily of white schizophrenic patients.[18,38–40] Additional studies should be undertaken to determine if this lower amount of weight gain also occurs in other Asian schizophrenic populations. Nevertheless, for patients taking olanzapine who do gain weight, recent findings show that a proper diet and behavioral changes such as attending support group meetings and starting an exercise program can significantly reduce weight gain.[41]

Even though the rate of successful switching was high in both groups, nearly one third of the patients did not experience a successful switch to olanzapine. A recent study found that 90.5% (76/84) of Hispanic patients (with schizophrenia, schizoaffective disorder, or schizophreniform disorder) were successfully switched to olanzapine from haloperidol.[36] However, the rate of successful switching was based only on those patients who completed the study. If we include only those patients who completed the study, then 88.8% of patients in the direct switch group were successfully switched from their previous medication. Thus, the findings are very similar between 2 ethnic groups and suggest that directly switching schizophrenic patients to olanzapine from other antipsychotics is effective and provides a favorable safety profile.

There have been reports of symptom or EPS exacerbation or worsening after abruptly stopping typical antipsychotic treatments to switch to another antipsychotic.[42,43] It has been recommended that start-tapering or cross-titration be implemented when switching patients to different antipsychotics.[31,42,43] However, in this study, there was a higher percentage of successful switches in the direct switch group than in the start-taper group. A recent study by Kinon and colleagues[32] found that if schizophrenic patients were either switched directly or start-tapered to olanzapine from typical antipsychotics or

risperidone, measurements of efficacy and treatment-emergent adverse events were very similar. These results suggest that most patients could be directly switched to olanzapine when a patient's present medication is unsatisfactory.

The large majority of patients in this study were switched to olanzapine from typical antipsychotics. Could patients who have had a suboptimal response to or who are experiencing unwanted side effects from an atypical antipsychotic be switched to olanzapine? The study by Kinon and colleagues[32] showed that patients on treatment with the atypical antipsychotic risperidone could be safely and effectively switched to olanzapine. Two studies[44,45] have shown that a majority of schizophrenic patients could be switched from clozapine to olanzapine and maintain or improve their psychotic symptomatology. Most patients also had a decline in drug-induced side effects. This successful switching was predicted on the basis of the similarity of the receptor-binding profile of olanzapine to that of clozapine. However, while some reports corroborate these findings,[46,47] other studies have found lower success rates when switching from clozapine to olanzapine.[48,49]

In comparison, some studies have shown that a number of patients had an exacerbation of psychotic symptoms or side effects when switching from clozapine to risperidone.[50,51] A study by Kirov and colleagues[52] found that risperidone was effective in most patients when switching from typical antipsychotics. In another study,[53] 6 patients with schizophrenia or schizoaffective disorder who were switched from sertindole to quetiapine showed only mild side effects, and none showed a worsening of symptoms. In 2 separate trials, patients with schizophrenia or schizoaffective disorder who had shown a partial response to olanzapine or risperidone were switched to ziprasidone via 1 of 3 switch strategies.[54] Patients in both groups showed statistically mean improvements in negative symptoms, and patients in the olanzapine group showed significant improvement in positive symptoms. However, the results were not separated by switch strategy and there was no mention of side effects (improvement or worsening) in the review article reporting these results. Therefore, the success of switching from one antipsychotic to another may depend on several factors including the current drug, the design of the switch, the dose of the new drug, the severity of psychotic symptoms and EPS, and other side effects related to the previous drug.

One limitation of this study was the lack of a comparison group that continued with their previous medications. It also would have been informative to have a comparative group that switched to another atypical antipsychotic such as risperidone or quetiapine. Another limitation is that the patients' duration of illness and length of drug treatment were not captured in this study. This information would have been helpful in classifying this population of schizophrenic patients. Finally, because the trial was open label, it was subject to observation bias. However, the purpose of this study was to closely imitate the normal treatment conditions of the clinical setting.

In conclusion, both the direct switch and start-taper switch groups showed significant improvement on all efficacy measures as well as for EPS and akathisia. These results suggest that, where indicated, changing Asian patients with a diagnosis of schizophrenia to olanzapine from another antipsychotic, by either a direct or gradual switch, may be a safe and effective therapeutic option.

Drug names: benztropine (Cogentin and others), chlorpromazine (Thorazine and others), clozapine (Clozaril and others), haloperidol (Haldol and others), olanzapine (Zyprexa), quetiapine (Seroquel), risperidone (Risperdal), ziprasidone (Geodon).

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