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Switching to paliperidone extended release in patients with schizophrenia dissatisfied with previous olanzapine treatment

Post hoc analysis of an open-label, prospective study

Tian Mei Si, MD[a,b], Shang Li Cai, PhD[c], Jian Min Zhuo, MS[d], Li Li Zhang, MMed[c,*]

Abstract

Objective: This post hoc analysis of an open-label, single-arm, multicenter study was designed to assess the efficacy, safety, and tolerability of paliperidone extended release (ER) in Chinese patients with non-acute schizophrenia, after switching from olanzapine.

Methods: Patients with schizophrenia who were dissatisfied with prior olanzapine treatment switched to flexible paliperidone ER (3–12 mg/day) based on clinical judgment. Change from baseline to week 12 in Positive and Negative Syndrome Scale (PANSS) total scores (primary endpoint), PANSS subscale scores, response rate, Clinical Global Impression-Severity (CGI-S) score, personal and social performance (PSP) scores, patient satisfaction with treatment score, change in sleep quality, level of daytime sleepiness and safety were evaluated.

Results: Out of 118 enrolled patients, 95 (81%) completed the study. Mean duration of study was 76.9 (23.85) days. The primary endpoint, mean (SD) PANSS total score changed significantly from baseline to endpoint (−19.6 [18.71], $P<.0001$). Secondary endpoints including PANSS subscale score, PSP, patient satisfaction and daytime drowsiness also significantly improved ($P<.001$). Most commonly reported (≥1%) treatment-emergent adverse events were akathisia (n = 14 [12%]) and insomnia (n = 9 [8%]).

Conclusions: Switching to flexible-dosed paliperidone ER in patients dissatisfied with prior olanzapine treatment achieved good efficacy and tolerability consistently over 12 weeks.

Abbreviations: CGI-S = Clinical Global Impression-Severity, DSM = diagnostic and statistical manual of mental disorders, EPS = extrapyramidal symptom, ER = extended release, FAS = full analysis set, PANSS = Positive and Negative Syndrome Scale, PSP = personal and social performance, TEAEs = treatment-emergent adverse events.

Keywords: antipsychotic, olanzapine, paliperidone extended release, schizophrenia, switching

1. Introduction

Over the past few decades, several antipsychotic agents have been established as mainstays for schizophrenia treatment.[1] However, clinical improvement and relapse prevention are often impeded by inadequate improvement or aggravation of symptoms, lack of efficacy and tolerability, partial or non-adherence to medication, relapse despite adherence to medication, impaired functioning, or patient decision.[2–6] Under these circumstances, switching antipsychotic medication is a common clinical practice to improve efficacy, tolerability, adherence, functioning and quality of life, while reducing hospitalization rates.[4,5]

Paliperidone extended-release (ER) (Invega; Janssen Pharmaceuticals, Inc.), an oral atypical antipsychotic, is approved for the acute and maintenance treatment of schizophrenia in the US, EU, China, and many other countries.[7–9] Earlier studies have demonstrated the efficacy and tolerability of paliperidone ER in patients with schizophrenia, delaying symptom recurrence in stable patients.[10–15]

In China, the prevalence of schizophrenia is reported to be about 781 out of 100,000 individuals.[16] Olanzapine, approved for the treatment of schizophrenia since 1998, is one of the most commonly used antipsychotic agents in China.[17] Although olanzapine has been shown to be effective in treating the positive and negative symptoms of schizophrenia,[18–20] earlier global studies have also reported undesirable metabolic effects with olanzapine. A pooled incidence of clinically significant weight gain (≥7%) was reported in 22% of patients on olanzapine, as reported in the US product label data of short-term treatment of generally 4 to 6 weeks.[21–23] Olanzapine has also been associated with insulin resistance.[24–28] A 52-week study directly comparing treatment with olanzapine and aripiprazole reported

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[a] National Clinical Research Center for Mental Disorders & The Key Laboratory of Mental Health, Ministry of Health (Peking University), [b] Peking University Institute of Mental Health/The Sixth Hospital, [c] Xian Janssen Pharmaceutical Co Ltd, Beijing, [d] Janssen Research & Development Center, Johnson & Johnson Investment Ltd, Shanghai, People's Republic of China.

[*] Correspondence: Li Li Zhang, Department: Medical Affairs, Xian Janssen Pharmaceutical Co Ltd, No.77, JianGuo Road, Chaoyang District, BeiJing, China 100025 (e-mail: lzhan212@its.jnj.com).

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significantly higher new-onset elevations in cholesterol and triglyceride levels; a higher percentage of patients reported clinically significant weight gain with olanzapine ($P \leq .05$).[29] In addition, the risk of metabolic syndrome has been reported to be higher with olanzapine.[30]

In this post hoc analysis, we examined the efficacy, safety, and tolerability of 12 weeks of paliperidone ER treatment in Chinese patients with non-acute phase of schizophrenia, who were not satisfied with the efficacy, or had tolerability issues, with previous olanzapine treatment.

2. Methods

2.1. Patients

Patients (men and women, age 18–65 years), with a diagnosis of non-acute phase of schizophrenia (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision [DSM-IV], criteria), with relatively stable state of illness were eligible for inclusion. Eligible patients receiving at least 6 to 8 weeks risperidone, olanzapine, or quetiapine at correct dose (dose range recommended by the instruction) and had to change medication due to lack of efficacy, poor tolerability, or other reasons were enrolled in the study. Major exclusion criteria were history of refractory schizophrenia; allergy to paliperidone ER or risperidone; history of substance dependence within 6 months before screening; history of neuroleptic malignant syndrome; tardive dyskinesia, or any malignancy. Patients who had received any long-acting injectable antipsychotic therapy within 1 month of screening were also excluded from the study. Only patients switch from olanzapine were included in this post hoc analysis.

3. Study design

This was a post hoc analysis of a 12-week, open-label, prospective, single-arm, phase 3b study conducted across 19 centers in China between July 2008 and September 2009 (NCT01541371).[31] Based on the major reasons for switching from olanzapine to flexibly-dosed paliperidone ER tablets, patients were divided into 3 groups: insufficient efficacy of prior olanzapine treatment (patients with PANSS total scores ≥70 at baseline or having ≥2 items in PANSS positive or negative subscale with ≥4 scores, or having ≥3 items in general psychopathology subscale with ≥4 scores), poor tolerability to olanzapine (as per physician/investigator's discretion or if patient had any treatment-emergence adverse event, TEAE) and any other reason for switching.

The study protocol was reviewed by an Independent Ethics Committee or Institutional Review Board, as appropriate, for each site (Supplementary information, http://links.lww.com/MD/C705). The study was conducted in compliance with the Declaration of Helsinki consistent with Good Clinical Practices and applicable regulatory requirements. Written informed consent was obtained from all patients before enrolment.

3.1. Medication dosing

Patients on prior olanzapine treatment had switched to flexibly-dosed paliperidone ER treatment either abruptly, or by attaining a reduction in olanzapine dosage gradually until discontinuation, within 2 weeks. Patients received 6-mg/day paliperidone ER as a starting dose, and the dose was subsequently adjusted, within a window of 3 to 12-mg/day based on clinical judgment.

3.2. Concomitant medications

Other antipsychotics were discontinued within 2 weeks after the initiation of this study. Antidepressants, mood stabilizers or a traditional Chinese medicine influencing the efficacy of oral paliperidone treatment were also not allowed during the study. Concomitant medications such as benzodiazepines or non-benzodiazepines, anticholinergics, or treatment for any new or existing physical diseases were permitted during the study.

3.3. Efficacy assessments

Primary efficacy endpoint was the change in Positive and Negative Syndrome Scale (PANSS) total score from baseline to end-of-study (12th week or last post-baseline visit). Secondary efficacy endpoints included change in PANSS subscale scores, response rate (percentage of patients with a ≥20% reduction of PANSS total scores at endpoint from baseline), Clinical Global Impression-Severity (CGI-S) score, personal and social performance (PSP) scores, patient satisfaction with treatment score (assessed by a 5-point scale: 1 = very satisfied, 2 = satisfied, 3 = neutral, 4 = dissatisfied, 5 = very dissatisfied) and changes in sleep quality and level of daytime sleepiness.

3.4. Safety assessments

Safety assessments included TEAEs, extrapyramidal symptom (EPS) rating scales, clinical laboratory tests, vital sign measurements, 12-lead electrocardiograms, and physical examination findings.

4. Statistical methods

4.1. Sample size determination

In the group of patients enrolled due to lack of efficacy with previous antipsychotics, poor tolerability or safety, and other causes, the primary objective was to observe 5-point changes in PANSS total scores from baseline to endpoint, regarded as the least difference at the level of clinical significance. For a standard deviation of 17, a power of 90% and significant level of 0.025 (1-sided), 124 patients were required to demonstrate the assumption that efficacy of paliperidone ER would be superior to prior treatment. To explore certain additional subgroups (e.g., prior treatment with olanzapine, risperidone, quetiapine; patients with the newly diagnosed schizophrenia; patients with prominent positive symptoms; patients with prominent negative symptoms etc.), considering there was an overlap among these subgroups, a sample size of about 500 patients (4–6 subgroups) was estimated for subgroup analysis. Overall, 405 patients had been enrolled in this study. Data from patients who were dissatisfied with prior treatment with olanzapine (n = 118 of 405 patients) were used to perform this post hoc analysis.

4.2. Analysis set

Of the patients who were dissatisfied with prior olanzapine use, all patients who received at least one dose of paliperidone ER tablets and had at least one efficacy evaluation were included in the full analysis set (FAS); Safety analysis set included all patients who received at least one dose of paliperidone-ER and had safety data generated.

5. Statistical analyses

The percentage of patients with at least a 20% efficacy improvement in PANSS total scores was provided. The changes

Table 1

Demographic and baseline characteristics (full analysis set).

	N = 118
Age (years), Mean (SD)	31.1 (10.77)
Sex, n (%)	
Female	65 (55)
Study duration with olanzapine, days	
Mean (SD)	78.5 (21.68)
Causes for switching drugs, n (%)	
Insufficient efficacy of prior olanzapine	57 (48)
Poor tolerability or safety of prior olanzapine	51 (43)
Other reasons	10 (9)

SD = standard deviation

from baseline to endpoint were analyzed by Wilcoxon signed rank test. A 2-sided alpha level of 0.05 was applied to detect statistical significance of the difference between endpoint value and baseline value. All analyses were conducted by Janssen–Cilag EMEA.

6. Results

Of the 118 patients in the FAS, 95 (81%) completed the 12-week study treatment; 23 patients (20%) were withdrawn. The most common reasons for study discontinuation were insufficient efficacy (n = 7 [30%]), adverse event (n = 5 [22%]), lost to follow-up (n = 4 [17%]), withdrawal of informed consent and protocol violation (n = 2 [9%] each) and other causes (n = 3 [13%]). Baseline characteristics of patients are summarized in Table 1. Mean (SD) study duration with paliperidone ER treatment was 76.9 (23.85) days.

6.1. Causes for switching to paliperidone ER

Out of the 118 patients, 57 (48%) patients switched due to insufficient efficacy to prior olanzapine, 51 (43%) patients switched due to poor tolerability to prior olanzapine, while 10 (9%) patients switched their treatment due to other causes including poor adherence (Table 1).

6.2. Dosing

Mean (SD) previous dose of olanzapine in patients switched to paliperidone ER due to insufficient efficacy was 11.8 (5.46) mg/day, poor tolerance/safety was 11.8 (6.15) mg/day or due to other causes was 10.5 (7.25) mg/day (Supplementary Table 1, http://links.lww.com/MD/C705). All patients received a starting dose of paliperidone ER 6-mg/day. Subsequently, patients were dosed within a range of 3 to 12-mg/day, based on the physicians' discretion. Mean (SD) dose of paliperidone ER at the end of the study (day 84) was 6.9 (2.20) mg/day, with patients switched to paliperidone ER due to insufficient efficacy was 7.41 (4.17) mg/day, poor tolerance/safety was 6.61 (2.67) mg/day or due to other causes was 8.10 (2.47) mg/day (Supplementary Table 1 and 2, http://links.lww.com/MD/C705).

6.3. Concomitant benzodiazepines

Total 34 of 119 (29%) patients in the safety analysis set received one or more benzodiazepines during the study. The most commonly used benzodiazepine was clonazepam (n = 22, 19%), followed by lorazepam (n = 5, 4%), and alprazolam (n = 4, 3%). Concomitant benzodiazepine treatment was given to 5 (4.2%) patients at baseline, 13 (10.9%) patients after 2 weeks and 16 (15.7%) patients at the last 4 weeks of study (day 57–84).

6.4. Effectiveness of switching to paliperidone ER

The primary efficacy outcome showed a statistically significant change from baseline to endpoint in PANSS total score for patients who switched from olanzapine (mean [SD]: baseline 68.0 [18.59]; change at endpoint: − 19.6 [18.71]) ($P < .0001$). Mean improvement in PANSS total score was statistically significant for both patients who switched from olanzapine due to insufficient efficacy (mean [SD]: baseline 77.5 [16.69]; change at endpoint: −26.4 [21.85]) and patients who switched due to poor tolerability to olanzapine (mean [SD]: baseline 59.8 [17.39]; change at endpoint: −14.5 [15.50]) ($P < .0001$). Mean subscale factor scores also significantly improved from baseline to endpoint for both subgroups (Table 2). Total response rate (≥20% efficacy improvement in PANSS total scores) in patients receiving prior olanzapine treatment was 59% (70/118; 95% CI: 50.46%–68.19%). The response rate observed in patients who switched due to insufficient efficacy was 61% (35/57) and in patients who switched due to poor tolerability was 55% (28/51) (Table 2). The mean (SD) CGI-S score at baseline was 3.9 (1.23), which was mild to moderate in severity and was reduced to 2.6 (1.10) at the endpoint ($P < .0001$). The mean (SD) PSP score was significantly improved from baseline to endpoint (mean [SD] change at endpoint: 13.1 [16.42]; $P < .0001$).

Improvements in quality of sleep showed an increasing trend but was not significant at endpoint ($P = .1130$). Reduction in daytime drowsiness from baseline to endpoint was significant for patients switching due to lack of efficacy, lack of tolerability and due to other causes ($P \leq .0001$) (Table 2).

Following paliperidone ER treatment, the percentage of patients who were "very satisfied" or "satisfied" with efficacy increased from baseline (23/117 [20%]) to end-of-study (60/105 [57%]). None of the patients were "very dissatisfied" with efficacy at end-of-study. In terms of tolerability, most of the patients after switching to paliperidone were "very satisfied" or 'satisfied' at end-of-study (62/106 [69%]) versus baseline (18/117 [16%]) (Supplementary Table 3, http://links.lww.com/MD/C705).

6.5. Safety and tolerability

Total 58 of 119 (49%) patients in the safety analysis set reported ≥1 TEAEs. The most commonly reported TEAEs (in ≥1% of patients) were akathisia (n = 14 [12%]) and insomnia (n = 9 [8%]) (Table 3). Seven patients (4%) discontinued the study due to TEAE (gastrointestinal disorder [n = 1]; suicide attempt [n = 1]; chest discomfort [n = 1]; decreased appetite, poor quality sleep, akathisia [n = 1]; rhinitis [n = 1]; nausea, dizziness, vertigo, [n = 1]; upper respiratory tract infection [n = 1]). Disease deterioration was reported in only one patient in the poor olanzapine tolerance group. A total of 38 patients (32%) reported EPS-related adverse events. The most commonly reported EPS-related adverse events (>5%) were acute dystonia (n = 8 [7%]), akathisia (n = 15 [13%]), and Parkinson's disease (n = 11 [9%]). Mean change (SD) from baseline to endpoint in Parkinson's disease, dysmyotonia, movement disorders and akathisia subscale score was −0.3 (2.81) ($P = .034$). There was no significant change in mean weight ($P = .5508$). Compared with baseline, only 5 patients (4%) experienced a weight gain over 7% at endpoint. Prolactin levels

Table 2

Key efficacy parameters (full analysis set).

	Total				Insufficient efficacy to Olanzapine				Poor tolerance to Olanzapine			
	N	Baseline mean (SD)	N	Endpoint mean change (SD)	N	Baseline mean (SD)	N	Endpoint mean change (SD)	N	Baseline mean (SD)	N	Endpoint mean change (SD)
PANSS total scores, n	118	68.0 (18.59)	118	−19.6 (18.71)*	56	77.5 (16.69)	50	−26.4 (21.85)*	51	59.8 (17.39)	45	−14.5 (15.50)*
Positive subscale	118	16.5 (6.62)	105	−5.7 (5.97)*	56	20.8 (7.22)	50	−7.0 (5.96)*	51	15.8 (6.22)	45	−3.5 (4.64)*
Negative subscale	118	18.0 (6.66)	105	−5.5 (5.51)*	56	19.3 (6.25)	50	−7.5 (6.26)*	51	13.9 (6.05)	45	−3.9 (5.90)*
General psychopathological symptom subscale	118	33.5 (8.98)	105	−9.5 (9.91)*	56	37.4 (8.99)	50	−11.9 (12.14)*	51	30.1 (8.01)	45	−7.1 (7.92)*
Positive symptoms factor	118	21.0 (7.00)	105	−7.0 (6.63)*	56	23.7 (5.88)	50	−8.56 (7.22)*	51	18.6 (7.24)	45	−5.6 (6.58)*
Negative symptoms factor	118	18.2 (7.06)	105	−5.84 (6.43)*	56	21.4 (7.96)	50	−7.5 (7.55)*	51	16.0 (6.22)	45	−3.8 (4.96)*
Sleep assessment scale—sleep quality	118	71.8 (24.03)	106	5.4 (28.93)**	56	64.3 (26.49)	50	11.6 (31.70)**	51	78.1 (21.83)	46	−0.2 (27.87)
Sleep assessment scale—daytime drowsiness	118	43.6 (24.3)	106	−21.5 (28.23)*	56	41.2 (24.61)	50	−20.6 (23.70)*	51	45.5 (25.06)	50	−22.2 (32.32)*
PSP scores	118	60.6 (14.71)	106	13.1 (16.42)*	56	53.6 (13.88)	50	16.9 (17.91)*	51	65.5 (13.82)	46	9.4 (15.61)*
CGI-S Scores- Severity of disease	117	3.9 (1.32)	104	−1.3 (1.43)*	56	4.5 (1.06)	50	−1.6 (1.51)*	51	3.3 (1.25)	45	−1.0 (1.35)*
Response rate (≥20% efficacy improvement in PANSS total scores), n (%)	–	–	118	70 (59.3%)	–	–	57	35 (61.4%)	–	–	51	28 (54.9%)

Note: Total group contained all patients who switched due to insufficient efficacy to Olanzapine, who switched due to poor tolerance to Olanzapine and who switched due to other reasons; Data of PANSS total scores in Total group were analyzed using LOCF and other data were analyzed using observed case.

CGI-S = Clinical Global Impression-Severity, PANSS = positive and negative symptom scale, PSP = personal and social performance, SD = standard deviation.

* $P < .0001$.

** $P < .05$.

showed a significant increase from baseline (mean [SD] change from baseline to day 84: 202.7 [297.94]; $P = .0391$) (Supplementary Table 4, http://links.lww.com/MD/C705); only one patient reported a prolactin-related TEAE (mild in severity), which was considered by the investigator as probably related to study drug.

Table 3

Summary of treatment emergent adverse events (safety analysis set).

n (%)	Total N = 119
Any TEAE	58 (49)
Most common TEAE (>1% of patients)	
Akathisia	14 (12)
Insomnia	9 (8)
Vertigo	4 (3)
Parkinsonism	4 (3)
Dystonia	4 (3)
Nausea	4 (3)
Muscle contractions involuntary	4 (3)
Dizziness	3 (3)
Transaminases increased	3 (3)
White blood cell count decreased	3 (3)
Hypertonia	2 (2)
Lipids increased	2 (2)
Fatigue	2 (2)
Headache	2 (2)
Constipation	2 (2)
Slow response to stimuli	2 (2)
Tremor	2 (2)
Chest discomfort	2 (2)
Depressed mood	2 (2)
Delayed menstruation	2 (2)

TEAEs = treatment emergent adverse events.

No patient had abnormal ECG findings after treatment. Mean (SD) change of corrected QTc interval on ECG from baseline to day 84 was −0.7 [24.47] ($P = .7857$). There was no significant change in fasting glucose, lipid profile and other laboratory parameters from baseline to end of study. No deaths were reported during this study.

7. Discussion

This post hoc analysis suggests that treatment with flexibly dosed paliperidone ER (3–12 mg/day) significantly decreased clinical symptoms and improved functional status in patients with schizophrenia, who were dissatisfied with prior olanzapine treatment due to insufficient efficacy or poor tolerability. Patients switched to flexibly-dosed paliperidone ER treatment either abruptly, or by attaining a reduction in olanzapine dosage gradually until discontinuation, within 2 weeks. A mean dose of 6 mg/day paliperidone ER was considered to be equivalent to 10 mg/day dose of previous olanzapine.[5,32] The clinical benefits of switching to paliperidone ER have been demonstrated in both acute and maintenance treatment. Results of an earlier study indicated that paliperidone ER significantly improved psychotic symptoms, disease severity and patient functioning (as measured by PANSS, CGI-S, and PSP scores, respectively) compared with those on placebo ($P < .05$), in patients with non-acute schizophrenia who switched to paliperidone ER (3–12 mg/day) from risperidone.[33] Other studies have also confirmed significant and clinically relevant improvements from baseline in PANSS total and subscale scores, patient functioning, sleep quality, and daytime drowsiness (all $P < .0001$) when switched to paliperidone ER from oral antipsychotics.[34,35] Furthermore, another randomized controlled study demonstrated comparable efficacy but reduced metabolic side effects with paliperidone ER compared with olanzapine.[23] In agreement with those earlier studies, the

current analysis demonstrates that the transition to paliperidone ER from olanzapine was associated with a significant reduction in PANSS total scores and all factor scores (positive, negative, hostility/excitement, cognitive, and anxiety/depression) during the 12-week study period, supporting the use of paliperidone as an alternative treatment option for patients who are dissatisfied with their antipsychotic therapy. Previous studies have demonstrated the effective outcome of paliperidone ER in terms of personal and social functioning, evaluated by PSP scale as well as symptomatic improvement.[11,12,15,36,37] In this study, the mean PSP score was significantly improved from baseline to endpoint, indicating that personal and social function of patients were improved during the 12-week period. The present findings are in accord with the results of several earlier studies of paliperidone ER.[11,12,15,36,37] Severity of illness assessed using CGI-S scale was also improved from baseline to endpoint in this study. This decrease in the severity of illness was consistent with an earlier study in another Asian population, which compared the efficacy of paliperidone ER with olanzapine for the treatment of schizophrenia.[38] Our results are also in agreement with 3 previous 6-week, double-blind, placebo-controlled studies in which the safety and efficacy of paliperidone ER were evaluated in patients with schizophrenia. Results had shown significant improvements in symptoms of schizophrenia as well as in personal and social functioning. The PANSS total score from baseline to endpoint compared with placebo was significantly better in paliperidone ER than placebo in all 3 studies for all doses tested (3, 6, 9, 12, and 15 mg).[11–13]

Sleep disorders are commonly associated with schizophrenia.[39] Sleep disruption including difficulty to fall asleep, unable to re-sleep after early wake-up, daytime drowsiness, deep sleep or slow wave sleep loss and rapid eye movement latency shortened were also reported in earlier studies, independent of the course of disease.[39,40] In addition to causing distress, the sleep disorders were accompanied by increased thought disorder and excited symptoms.[41–43] Previous studies have shown that olanzapine possesses sedative and anticholinergic properties.[44] When switching from a sedating antipsychotic with higher affinity for cholinergic or histaminergic receptors like olanzapine to a non-sedating one with lower affinity like paliperidone may result in transient rebound insomnia. In such a scenario, short-term use of concomitant benzodiazepine may be recommended to control the insomnia.[5] Nevertheless in this study, with ~30% of patients treated with concomitant benzodiazepine, a trend towards improvement in sleep quality was reported, although not significant. Daytime drowsiness may have an adverse impact on patients' normal functioning.[45,46] The mean change in daytime drowsiness score from baseline to endpoint (day 84) showed significant improvement in daytime drowsiness, which in turn has a positive impact on the functionality outcome. The results suggest that paliperidone ER-retained patients' sleep quality, while daytime drowsiness was significantly decreased after switching from olanzapine.

No new safety findings were reported during the 12-week treatment period. Adverse events were reported in 60% of patients (n=71), which were comparable with previous studies.[11–15] Previous studies had identified increased prolactin levels as a common adverse event associated with paliperidone ER.[11,13] In this study, though prolactin increased significantly, the incidence of prolactin-related TEAEs was lower than previously reported.[47] Previous studies had reported substantial negative metabolic effects with olanzapine, which has been linked to insulin resistance, dyslipidemia, and excess weight gain.[48,49] However, paliperidone ER has a lesser effect not only on metabolism but also on weight gain, compared with olanzapine.[50,51] In this study, the incidence of weight gain and extrapyramidal disorder related assessments were low in patients after switching to paliperidone treatment. There was no sign of increased EPS events after switching from olanzapine to paliperidone ER. No significant changes in laboratory metabolic parameters were reported. In general, treatment with paliperidone ER was tolerable with a safety profile generally consistent with other marketed paliperidone formulations.

There are some limitations to this study. This was a post hoc analysis that was not designed to examine patients who had been previously treated with olanzapine; however, a population of patients was identified who had recently been exposed to olanzapine and yet were sufficiently symptomatic to meet entry criteria for this study. The elaborate safety data for subgroups based on reasons for switching is not available and hence it is difficult to generalize the safety findings to the subgroups although overall the switching from olanzapine to paliperidone ER was tolerated well and there were no new safety concerns observed in the study. This was an open-label design with no comparator drugs or a placebo. Also, this study was not powered to determine differences between prior medications, and larger sample sizes will be needed to confirm results. Further studies are warranted in these patients to better understand different approaches of switching considering the anticholinergic characteristics of olanzapine.

In summary, this study demonstrates that switching to flexible paliperidone ER (3–12 mg per day oral) in patients dissatisfied with prior olanzapine treatment achieved consistently good efficacy and tolerability over 12 weeks. Switching from previously unsuccessful antipsychotic treatments to paliperidone ER can thus be a useful option to achieve long-term improvement in symptoms and functioning for patients with schizophrenia.

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Author contributions

Tian Mei Si contributed towards the primary idea and the key analysis factors of this post-hoc analysis. Shang Li Cai and Li Li Zhang were responsible for design, data analyses and data interpretation. Jian Min Zhuo was responsible for statistical analyses. All authors meet ICMJE criteria and all those who fulfilled those criteria are listed as authors. All authors had access to the study data, provided direction and comments on the manuscript, made the final decision about where to publish these data, and approved submission to the journal.

Conceptualization: Zhang Li Li, Tian Mei Si, Shang Li Cai, Jian Min Zhuo.
Data curation: Zhang Li Li, Shang Li Cai, Jian Min Zhuo.
Formal analysis: Zhang Li Li, Jian Min Zhuo.
Investigation: Zhang Li Li, Tian Mei Si, Shang Li Cai.

Methodology: Zhang Li Li, Shang Li Cai, Jian Min Zhuo.
Project administration: Tian Mei Si, Shang Li Cai, Jian Min Zhuo.
Supervision: Zhang Li Li, Tian Mei Si.
Validation: Zhang Li Li, Shang Li Cai, Jian Min Zhuo.
Writing – original draft: Zhang Li Li, Tian Mei Si, Shang Li Cai, Jian Min Zhuo.
Writing – review & editing: Zhang Li Li, Tian Mei Si, Shang Li Cai, Jian Min Zhuo.

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