

Treatment of Patients with Recently Exacerbated Schizophrenia with Paliperidone Palmitate: A Pilot Study of Efficacy and Tolerability

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Background: Paliperidone palmitate is a long-acting, second-generation antipsychotic (SGA) indicated for the treatment of acute exacerbations and maintenance treatment of adults with schizophrenia. This study addressed the response to paliperidone palmitate in Latin American patients with acute symptoms and recently diagnosed schizophrenia.

Objective: Explore the efficacy and tolerability of paliperidone palmitate administered once a month for 4 months in patients with acute phase and recent diagnosis (within 1–6 years) of schizophrenia in 3 Latin American countries.

Methods: This was a non-randomized, open-label, multicenter study with paliperidone palmitate injected intramuscularly in the deltoid muscle at an initial loading dose of 150 mg eq. (234 mg) on day 1 and 100 mg eq. (156 mg) on day 8 (\pm 4 days). The recommended maintenance dose was 75 mg eq. (117 mg) from day 36 to day 92. Efficacy was evaluated with PANSS and CGI-S. The last observation carried forward (LOCF) was used for efficacy analysis for imputation of missing data; no adjustments were made for multiplicity. Adverse events were evaluated during treatment.

Results: The patient retention rate was 84.0% (144 patients received study drug; 121 finished the study). The percentage of patients with a reduction of at least 30% in PANSS total score compared to baseline gradually increased during the study, and at the end, 78.4% of patients showed response. The PANSS total score and CGI-S scores decreased significantly from baseline to LOCF endpoint ($P < 0.0001$ for both); significant reduction in PANSS total score was observed at day 8 and persisted to the end of the study. Most common adverse events were muscle rigidity (11.8%), akathisia (11.1%), injection-site pain (7.6%), weight gain (7.6%), and insomnia (7.6%).

Conclusion: Paliperidone palmitate was efficacious in Latin American patients studied with an acute exacerbation and recent diagnosis of schizophrenia, and no new safety signals were identified.

Keywords: paliperidone palmitate, recent onset, acute phase, schizophrenia

Introduction

Treatment adherence is one of the main problems in chronic diseases, given that approximately 60% of patients with chronic diseases show poor treatment adherence.¹ Adherence plays a key role in achieving a better prognosis in the treatment of schizophrenia.²

Antipsychotics are the primary treatment for controlling acute psychotic episodes and preventing relapses in the long term.^{3,4} However, schizophrenia is accompanied by high relapse and rehospitalization rates, with poor adherence

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being one of the main associated factors.⁵ Approximately 84% of patients with schizophrenia discontinue antipsychotic medication during treatment,⁶ and 40% to 50% of patients do not adequately comply with treatment in the long term.⁷ These percentages are similar between patients receiving first-generation antipsychotics (FGAs) and those receiving second-generation antipsychotics (SGAs).⁸

Eighty-two percent of patients diagnosed with a first episode of schizophrenia or schizoaffective disorder have at least one relapse during the first 5 years after initial recovery, and the risk of relapse is increased 5-fold in patients discontinuing treatment.⁹ On the other hand, over 35% of patients entering treatment have problems following the treatment protocol within the first 6 weeks, and non-adherence increases up to 75% after 2 years of treatment.^{10,11}

Depot FGAs were introduced in the 1960s and were developed with the goal of improving adherence; however, their effect on negative symptoms was absent or modest, and their association with side effects, such as extrapyramidal symptoms and increased prolactin levels, limited their use over time.¹² In recent years, long-acting injectable (LAI) SGAs have appeared as an alternative to increase adherence and improve prognosis, while decreasing side effects.^{13–15} In a systematic review of long-term studies, FGAs and SGAs were reported to reduce relapse rates in outpatients with schizophrenia from an average of 33.2% to 21.5%.¹⁶

Although the evidence indicates a decrease in relapse rates and better treatment compliance with LAI antipsychotics, their prescription is limited by a lack of knowledge about the use of these dosage forms and the preconceived notion that they are only suitable for a specific group of patients, usually chronic and severe patients and those with poor adherence.^{17,18} Additionally, LAI antipsychotics are generally not prescribed to patients with a first psychotic episode or recent-onset schizophrenia, although non-adherence is closely linked to relapse during these phases.¹⁹ Apparently, the low prescription rates of these therapeutic options are related to an alleged aversion of injectable medication in patients with a first episode and negative attitudes associated with the use of LAI antipsychotics.^{20–22} Nevertheless, published literature suggests that LAI SGAs represent a promising solution because they are associated with fewer adverse effects and present adequate efficacy for reducing symptoms and relapse rates.^{15,23} This has led to a gradual increase in the prescribing of these drugs, while their adoption is

still slow in some regions, such as Latin America.²⁴ The aim of this open-label study was to explore the efficacy and tolerability of paliperidone palmitate administered once a month for 4 months in patients with acute-phase schizophrenia in 3 Latin American countries.

Patients and Methods

Study Population

Patients were recruited from outpatient and inpatient services in Mexico, Colombia, and Brazil ([Supplemental Table 1](#)). The study included men and women who were not pregnant or lactating between 18 and 40 years of age (inclusive) with a diagnosis of schizophrenia for at least 1 year but less than 6 years (ie, recent-onset) according to the criteria of the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)*²⁵ confirmed by the Mini International Neuropsychiatric Interview (MINI) Spanish Version 5.0.0²⁶ or Brazilian validated version 5.0.²⁷ Patients were also required to have an acute exacerbation of psychosis lasting less than 4 weeks but more than 4 days, with a Positive And Negative Syndrome Scale (PANSS) total score of 70 to 120 (inclusive), and a score of 4 (moderately ill) or more on the Clinical Global Impression–Severity (CGI-S) scale at screening. All patients or their legally acceptable representatives provided signed informed consent prior to the study. The main exclusion criteria were a diagnosis of substance dependence (except nicotine and caffeine) according to the DSM-IV within 6 months prior to entry, treatment with an LAI antipsychotic within 3 injection cycles prior to baseline, a change of more than 10% in PANSS total score between screening and baseline assessment after the oral tolerability test, history of treatment resistance, history of malignant neuroleptic syndrome, history or current symptoms of tardive dyskinesia, any unstable systemic disease, and plans to conceive a child while enrolled in the study or within 50 days after the last dose of the drug under study.

An Independent Ethics Committee or Institutional Review Board at each study site ([Supplemental Table 1](#)) approved the protocol, and the study was carried out in accordance with the ethical principles in the Declaration of Helsinki and was consistent with Good Clinical Practices and applicable local regulations. This study was registered at ClinicalTrials.gov: NCT01448720.

Study Design

This was a non-randomized, open-label, multicenter study of paliperidone palmitate administered in a flexible dose

regimen in patients with an acute exacerbation of schizophrenia from 3 countries in Latin America. The study consisted of 2 phases: a screening phase of up to 4 days and a treatment phase of 4 months (injections were administered from day 1 to day 92 at monthly intervals followed by a visit at the end of the study on day 120) without an extension phase.

Study Medication

Paliperidone palmitate was administered intramuscularly and according to the regimen approved in the United States for the initiation and maintenance of treatment, with an initial loading dose of 150 mg eq. (234 mg) on day 1 and 100 mg eq. (156 mg) on day 8 (\pm 4 days) in the deltoid muscle. The recommended maintenance dose was 75 mg eq. (117 mg) from day 36 to day 92 at monthly intervals in the deltoid or gluteal muscle at the discretion of the investigator, depending on tolerability. This maintenance dose could be increased or decreased at the discretion of the investigator based on efficacy in a range between 50 mg eq. and 150 mg eq. (flexible maintenance dose scheme).

Patients without prior exposure to risperidone or paliperidone were administered 1 mg/day of oral risperidone or 3 mg/day of extended-release (ER) OROS[®] paliperidone for at least 3 days in the screening phase, before the first injection of study drug for tolerability testing. Administration of other antipsychotics was allowed during the study at the discretion of the investigator, as was concomitant therapy with mood stabilizers, anticholinergics, benzodiazepines, hypnotics, or antidepressants.

Assessments

Efficacy was assessed at screening and on days 1, 4, 8, 36, 64, 92, and 120 (final assessment). Only qualified and trained raters (psychiatrists, psychiatry residents, or psychologists) who had ≥ 3 years of experience evaluating patients with schizophrenia administered the PANSS. The primary efficacy endpoint was the proportion of patients with response to treatment, defined as the percentage of patients with a PANSS total score reduction of $\geq 30\%$ at the final assessment compared to baseline.²⁸ The 30-item PANSS provided a total score (sum of the scores of all 30 items) and scores for 3 subscales: the positive syndrome subscale (7 items), the negative syndrome subscale (7 items), and the general psychopathology subscale (16 items). Each question was rated on a scale of 1 (absent) to 7 (extreme).

Secondary efficacy endpoints were changes from baseline at each time point in PANSS total score and PANSS Marder factor scores²⁹ and CGI-S score.³⁰ Additionally, the time to treatment failure was defined as the time to psychiatric hospitalization, presence of suicidal behavior, or discontinuation of the study drug due to lack of efficacy or safety or tolerability problems, at the discretion of the investigator.

Safety assessments performed during the study included adverse events, body weight/body mass index, assessment of extrapyramidal symptoms using the Abnormal Involuntary Movement Scale (AIMS),³¹ and presence of suicidal behavior using the InterSePT Scale for Suicidal Thinking–Plus (ISST-Plus).³² During screening and at the end of the study, lipid profile and fasting glucose were measured, and an electrocardiogram was performed.

Statistical Analysis

The size of the current sample was not based on any statistical power calculation because it was an exploratory study. A sample size of 150 patients entering the study was deemed to be sufficient to allow for a preliminary exploration of safety and efficacy in this open-label, single-arm study. Efficacy analyses were performed on the intent-to-treat (ITT) population, which included all patients who received at least 1 dose of study drug. Categorical variables are presented as number and percentage of patients, and continuous variables are summarized using means and standard deviations (SDs). The last observation carried forward (LOCF) was used for the efficacy analysis for imputation of missing data. No adjustments of type I error for multiplicity were planned in order to account for multiplicity of primary variables.

Patients who showed a reduction in PANSS total score $\geq 30\%$ were considered responders. The response was analyzed at each measurement point, including LOCF criteria. The time to first response (ie, reduction of $\geq 30\%$ from baseline in PANSS total score), expressed as the number of days from the first injection until the first response, was analyzed using the Kaplan–Meier method.

Secondary efficacy was assessed using a paired *t*-test to establish differences in the change from baseline. The level of statistical significance was set at $P < 0.05$, with 95% confidence intervals (CIs).

Safety parameters were reported from observed data (without imputation) for the ITT population.

The data sharing policy of Janssen Pharmaceutical Companies of Johnson & Johnson is available at <https://www.janssen.com/clinical-trials/transparency>. As noted on

this site, requests for access to the study data can be submitted through Yale Open Data Access (YODA) Project site at <http://yoda.yale.edu>.

Results

Patient Disposition, Baseline Demographics, and Clinical Characteristics

The initial study population was 151 patients, excluding 7 patients who did not receive the study drug. Thus, 144 patients were included in the ITT analysis. There was a predominance of men ($n = 101$, 70.1%), the mean age was 26.8 years ($SD = 6.2$; range, 18–41 years), the mean age of onset of the first psychotic episode was 23.6 years ($SD = 6.1$; range, 13–38.1 years), and the average time from DSM diagnosis to baseline was 2.9 years ($SD = 1.3$; range, 0.0–5.8 years). Twenty-five (17.4%) patients reported having a psychiatric history, of which depression and drug abuse were most common, each occurring in 6 patients, and insomnia occurred in 3 patients. Previous hospitalization was reported for 75 (52.1%) patients, but most patients (128/144 [88.9%]) entered the study as outpatients, with a mean time since last hospitalization of 31.2 days ($SD = 49.0$ days).

Enrolled patients had an acute psychotic episode reflected by a mean baseline PANSS total score of 95.1 ($SD = 14.7$) and a mean CGI-S of 4.8 ($SD = 0.7$). Mean time-to-readiness for discharge in the ITT hospitalized population was 40.0 days ($SD = 23.0$; range, 13–73 days).

The patient retention rate in the study was 84.0%; 121 patients finished the study. The most common reasons for discontinuation were withdrawal of consent (5.6%), treatment failure (3.5%), adverse event (2.8%), and loss to follow-up (2.1%).

Treatment Exposure and Concomitant Treatment

Tolerability testing was performed in 64 patients (44.4%); of these, 47 patients received risperidone (73.4%) and 17 received paliperidone ER (26.6%). The patients received an average of 5 injections ($SD = 1$; range, 2–5). The mean time from baseline to the last application of paliperidone palmitate was 86 days ($SD = 23$; range, 10–107 days).

The mean maintenance dose of paliperidone palmitate (after excluding the higher doses given at day 1 and day 8) was 96.84 mg at day 92.

In the ITT population, 55 (38.2%) patients had received previous psychotropic medications and 88 (61.1%) patients were receiving concomitant psychotropic medications at baseline evaluation (Table 1). Mean doses of previous (at baseline) and current psychotropic medication decreased during the study, but the difference was not statistically significant. The most common antipsychotics that patients initiated during the study were oral

Table 1 Previous and Final Psychotropic Treatment, ITT Population (N = 144)

Medication	Previous n (%)	End of Study n (%)
Antipsychotics		
Aripiprazole	1 (0.7)	1 (0.7)
Chlorpromazine	3 (2.1)	4 (2.8)
Clozapine	0	1 (0.7)
Haloperidol	18 (12.5)	2 (1.4)
Levomepromazine	3 (2.1)	7 (4.9)
Olanzapine	13 (9.0)	13 (9.0)
Paliperidone	0	4 (2.8)
Pipotiazine	1 (0.7)	0
Promethazine	5 (3.5)	6 (4.2)
Quetiapine	5 (3.5)	3 (2.1)
Risperidone	30 (20.8)	30 (20.8)
Sertindole	1 (0.7)	0
Amisulpride	0	1 (0.7)
Sulpiride	1 (0.7)	0
Thioridazine	1 (0.7)	0
Trifluoperazine	1 (0.7)	0
Zuclopenthixol	1 (0.7)	0
Benzodiazepines		
Alprazolam	0	2 (1.4)
Clonazepam	6 (4.2)	21 (14.6)
Diazepam	4 (2.8)	6 (4.2)
Eszopiclone	0	2 (1.4)
Lorazepam	5 (3.5)	20 (13.9)
Midazolam	0	1 (0.7)
Nitrazepam	1 (0.7)	0
Anticholinergics		
Biperiden	9 (6.3)	31 (21.5)
Antidepressants		
Fluoxetine	2 (1.4)	4 (2.8)
Paroxetine	1 (0.7)	1 (0.7)
Sertraline	1 (0.7)	5 (3.5)
Mood Stabilizers		
Lithium	3 (2.1)	3 (2.1)
Carbamazepine	0	1 (0.7)
Topiramate	1 (0.7)	0
Valproic acid	3 (2.1)	0

paliperidone and levomepromazine ($n = 4$ each). Injectable and oral FGA treatments were reduced during the study. Benzodiazepines, anticholinergics, and antidepressants tended to be prescribed to a greater number of patients after starting the study. On the other hand, the prescription of mood stabilizers showed little change (Table 1).

Efficacy

The percentage of patients with a reduction of $\geq 30\%$ in PANSS total score from baseline gradually increased during the study, with 59.6% of patients showing response after 36 days and 78.4% of patients showing response at LOCF endpoint visit (Figure 1). The mean time to response according to the criterion of a $\geq 30\%$ reduction in PANSS total score from baseline was 48.5 days ($SD = 2.93$; 95% CI, 42.75 to 54.22), and the estimated median time to response was 35 days (interquartile range, 34–66 days).

Treatment failure according to our pre-established criteria occurred in 14 (9.7%) patients an average of 54.0 days ($SD = 38.0$; range, 2–123 days) after the first dose. Reasons for treatment failure were: 6 (4.2%) substantial clinical deterioration, 5 (3.5%) treatment discontinuations due to lack of efficacy, 4 (2.8%) suicidal behavior, and

3 (2.1%) treatment discontinuations due to safety or tolerability concerns (patients may have 2 different reasons).

The PANSS total score decreased significantly during the study, with a mean change from baseline to endpoint [LOCF] of -32.7 ($SD = 22.1$; 95% CI, -36.4 to -29.0 ; $P < 0.0001$) (Figure 2). Statistically significant changes were also observed from baseline in CGI-S score at each visit and at LOCF endpoint ($P < 0.0001$). There was an early onset of antipsychotic effect, reducing symptoms in 8 days (PANSS total score change at day 8 from baseline = -12.6 ; $SD = 13.4$; 95% CI, -14.8 to -10.4 ; $P < 0.0001$).

Safety

Safety analysis was performed on the ITT population ($n = 144$). During the study, 63.9% of patients reported at least 1 adverse event. The most common adverse events were muscle rigidity (11.8%), akathisia (11.1%), pain associated with the injection (7.6%), weight gain (7.6%), and insomnia (7.6%; Table 2). Two (1.4%) serious adverse events were recorded, 1 psychotic episode and another patient with weight loss. Four (2.8%) patients had 5 adverse events that resulted in treatment discontinuation: agitation, akathisia, hyperglycemia, psychotic disorder, and weight decrease. Mean body weight at baseline was 73.6 kg ($SD = 17.3$); mean body weight at endpoint was 75.6 kg ($SD =$

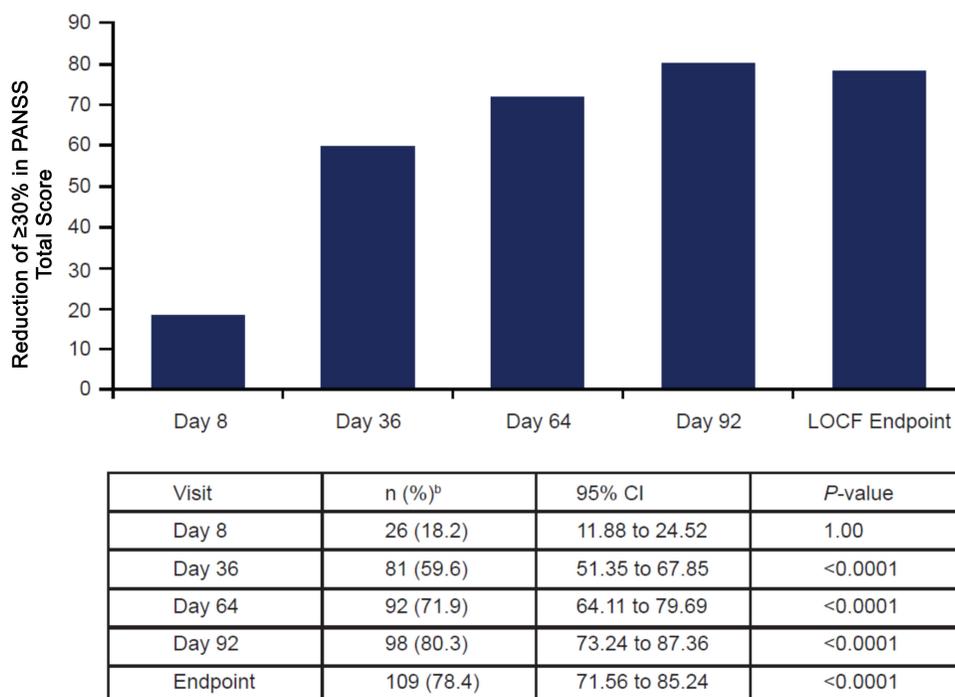


Figure 1 Reduction of $\geq 30\%$ in PANSS total score with respect to baseline visit: LOCF/ITT population^a. ^aP-value corresponds to the test of hypothesis of $P = 0.35$ on each visit; ^bNote that not all patients in the ITT population had efficacy data at each time point evaluated and thus the total “n” at each visit is not always the total population of 144 patients.

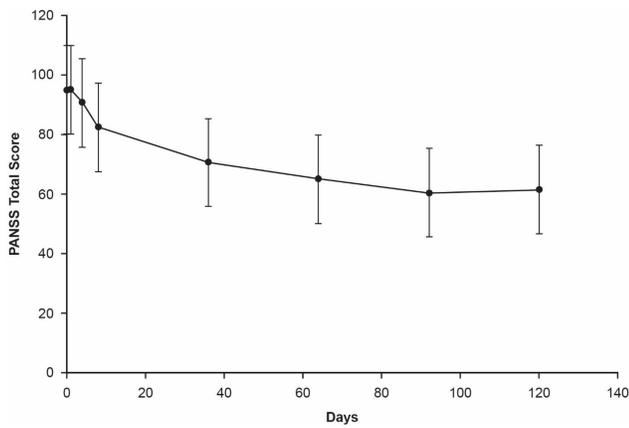


Figure 2 PANSS total scores over time in the ITT population. Mean (\pm SD) based on raw score with 15% imputation rule applied on every point.

17.9). One adverse event was associated with increased prolactin (0.7%).

The occurrence of extrapyramidal symptoms (eg, tardive dyskinesia) measured by the AIMS was low (<4%) during the study, with a baseline mean (SD) of 0.4 (1.2) and an endpoint mean (SD) of 0.6 (2.1). No significant clinical changes were found at endpoint in relation to baseline in vital signs, laboratory parameters (including fasting glucose and lipid profile), or ECG recordings.

Discussion

In 3 Latin American countries, patients with recent-onset schizophrenia (diagnosis within 6 years of study

Table 2 Treatment-Emergent Adverse Events (ITT Analysis Set; N = 144)

Most Common Adverse Events	n (%)
≥ 1 TEAE	92 (63.9)
EPS-related TEAEs	
Muscle rigidity	17 (11.8)
Tremor	8 (5.6)
Parkinsonism	2 (1.4)
Dystonia	4 (2.8)
Dyskinesia	2 (1.4)
Akathisia	16 (11.1)
Injection site pain	11 (7.6)
Weight increase	11 (7.6)
Insomnia	11 (7.6)
Somnolence	9 (6.3)
Anxiety	8 (5.6)
Headache	7 (4.9)

Abbreviations: TEAE, treatment-emergent adverse event; EPS, extrapyramidal symptom.

screening) starting paliperidone palmitate intramuscularly (following prescription recommendations) during an acute episode of psychosis and subsequently treated with a monthly dose of 75 mg eq. (117 mg) had improved clinical symptoms and overall disease status. A high proportion of patients responded to treatment with adequate tolerability.

These results are similar to randomized, placebo-controlled studies of paliperidone palmitate performed in patients with acute schizophrenia in other regions.^{33,34} A recent subgroup analysis of 2 large phase 3 trials supported the efficacy and safety of paliperidone palmitate every 3 months in Latin American patients,³⁵ showing that more than 90% of patients remained relapse-free over 48 weeks. Patients with acute symptoms of schizophrenia and unsuccessful treatment with oral antipsychotics received paliperidone palmitate in an open-label, 6-month study in 21 countries across Europe and the United Kingdom.³⁶ Two-thirds of patients achieved $\geq 30\%$ reduction in mean PANSS total score, with significant reductions observed as early as day 8. A recent systematic review of monthly paliperidone palmitate in real-world evidence studies concluded that the treatment provides consistent results of reducing relapse-related events, including hospitalizations.³⁷

The dosing regimen for paliperidone palmitate used in this study, with an initial loading dose of 150 mg eq. (234 mg) on day 1 and 100 mg eq. (156 mg) on day 8 in the deltoid muscle, followed by a monthly maintenance dose of 75 mg eq. (117 mg), produced a fast reduction in PANSS total score that was statistically significant at day 8 and persisted to the end of the study. This finding supports the early onset of antipsychotic effect after the first injection of paliperidone palmitate 150 mg eq. and is consistent with what has been reported in previous studies.^{38–40} However, it is important to remember that the study allowed for the prescription of other antipsychotics, and their effect cannot be ruled out as potentiators of the response.

Between 2.3% and 9.3% of patients with newly diagnosed schizophrenia treated with paliperidone palmitate have extrapyramidal symptoms.^{41,42} Akathisia has been reported with a frequency of 1.9% in previous studies, being higher in patients with chronic schizophrenia.⁴² Compared with these previous reports, the frequencies of extrapyramidal symptoms (12.5%) and akathisia (11.1%) were higher in this study and were most likely related to the maintenance of other antipsychotic therapies and to the fact that oral paliperidone was added for some patients.

During the study, FGA oral and injectable antipsychotics were discontinued or reduced, while oral SGAs risperidone, olanzapine, and aripiprazole were unchanged. The use of other antipsychotics varied but only in a small proportion of the study population. This pattern of prescribing oral antipsychotics in conjunction with the proposed regimen for paliperidone palmitate could also be related to the increase in the use of concomitant therapy, mainly with biperiden and benzodiazepines for the management of extrapyramidal symptoms and akathisia. Additionally, because patients received paliperidone palmitate until the last observation and there was no extension phase, it is unknown whether tardive dyskinesia occurred after discontinuation of the study drug. Other adverse events reported were pain at the injection site, weight gain, insomnia, drowsiness, headache, and anxiety. Adverse events were similar to those observed in other studies with paliperidone palmitate.^{42,43}

It has been suggested that LAI antipsychotics may be a particularly suitable treatment option for patients with early schizophrenia. The first 5 to 10 years of the disease are critical to establish an adequate control of symptoms to help prevent clinical deterioration and reduce the risk of relapse due to non-adherence.^{44,45} Patients with recent schizophrenia are likely to have treatment adherence problems due to lack of insight regarding their illness and their need for treatment. They are also likely to lack social support and to abandon treatment by their own choice.⁴⁶ On the other hand, in the early stages of schizophrenia, a better response to antipsychotic treatment⁴⁷ and increased susceptibility to adverse events⁴⁸ are observed. The presence of adverse events is another factor associated with treatment discontinuation in patients with recent schizophrenia. The recommendation to start with an initial loading dose of 150 mg eq. of paliperidone palmitate, followed by a dose of 100 mg eq. on day 8 in the deltoid muscle, and a monthly maintenance dose of 75 mg eq., could raise concerns of causing more side effects in patients with early-stage schizophrenia. The International Clinical Guidelines for Early Psychosis and the World Psychiatric Association recommend the minimum effective dose whenever possible.⁴⁹

Our use of a loading dose of paliperidone palmitate was based on reports of its efficacy and tolerability.^{34,50} Lower initial doses administered in the gluteal muscle may lead to subtherapeutic plasma levels and poor long-term response in schizophrenia.⁵¹ This study reported an excellent retention rate (84%), a good response, and a suitable

tolerability profile. However, it is not possible to rule out the effect of oral antipsychotics prescribed during the study on treatment efficacy and the increase of some adverse events.

Data interpretation in this study is limited by the use of an open-label design, the short duration, the limited number of patients, and the lack of a comparison group. As this was an exploratory study, the intention was not to compare treatment with paliperidone palmitate to another treatment (eg, comparator or placebo). Additionally, the fact that oral antipsychotics were maintained and concomitant therapy with anticholinergics, benzodiazepines, mood stabilizers, and antidepressants was allowed during the study could lead to bias in the interpretation of the efficacy and safety results. Moreover, 5 patients started on new oral antipsychotics during the treatment phase, and doses of current antipsychotics could be changed during the study. While this open-label design and use of concomitant medications reflect current real-world clinical practice for the management of patients with recent schizophrenia during an acute episode, it is a very significant limitation of the study. Together, these factors limit the strength of the conclusions and the generalization of the efficacy and safety of paliperidone palmitate in patients with an acute episode of schizophrenia in a Latin American population (Mexico, Colombia, and Brazil).

It is worth highlighting the pattern observed for the prescription of oral antipsychotics during the study, as it could reflect a lack of confidence in the clinical efficacy of LAI SGAs in the early phases of the disease and in acute episodes of psychosis. One of the main barriers to the initiation of treatment with LAIs is that psychiatrists often assume that patients with a first episode of psychosis or early schizophrenia would reject injectable antipsychotics. Psychiatrists believe it would be difficult to convince patients of the need, as they have not yet experienced relapses. Patients may also regard the treatment as a coercive measure, so psychiatrists often reserve this therapy for chronic patients.⁵² There is a high relapse rate in the early phases of schizophrenia, and LAI SGAs are a valid therapeutic option considered in the clinical guidelines.⁵³ However, their use is limited due to several reasons, including physician reluctance to change prescribing habits, lack of physician knowledge on how to use these forms of drugs, and the misconception that LAI SGAs should only be used in a very specific group of people (ie, severely ill patients and those who have shown poor adherence).^{17,18,20-22,54}

Conclusions

Results of this study demonstrated that paliperidone palmitate has an early onset of action in patients with an acute episode of schizophrenia. Paliperidone palmitate was efficacious at the recommended doses and no new safety signals were identified. Finally, we suggest performing studies on the perception of psychiatrists regarding treatment with LAI SGAs in recently diagnosed patients and reviewing existing management guidelines in Latin America (Mexico, Colombia, and Brazil) due to the observed pattern of prescription of oral antipsychotics with paliperidone palmitate.

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Author Contributions

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

Disclosure

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