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ORIGINAL RESEARCH

Long-Term Symptomatic and Functional Remission with Paliperidone Palmitate 6-Monthly Treatment in Schizophrenia: A 3-Year Post-Hoc Analysis

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Purpose: Long-acting injectable (LAI) formulations of paliperidone palmitate (PP) 1-month-(PP1M), 3-month-(PP3M), and 6-month-(PP6M) have been shown to delay time to relapse and to lower relapse rates, while maintaining symptomatic and functional improvements in patients with schizophrenia. This post-hoc analysis assessed symptomatic and functional remission rates in patients who transitioned from PP3M to PP6M (PP3M/PP6M) or continued PP6M (PP6M/PP6M) over 3 years.

Methods: Adult patients with schizophrenia, clinically stable on moderate/high doses of PP1M or PP3M, were randomized to PP6M or PP3M during the 12-month double-blind (DB) phase of a phase-3, noninferiority trial (NCT03345342). Eligible patients who remained relapse-free at the end of the noninferiority trial could choose to continue PP6M in a 2-year, single-arm, open-label extension (OLE) study (NCT04072575). Symptomatic remission was assessed using the Andreasen criteria (Positive and Negative Syndrome Scale symptoms [P1,G9,P3,P2,G5,N1,N4,N6] score of ≤3 for ≥6 months), while functional remission was defined as Personal and Social Performance score >70.

Results: A total of 178 patients either transitioned to PP6M (PP3M/PP6M=57) or continued PP6M (PP6M/PP6M=121) treatment in the OLE study. At the 1-year DB endpoint, 47/57 (82.5%) PP3M/PP6M patients and 103/121 (85.1%) PP6M/PP6M patients achieved symptomatic remission, while 30/57 (52.6%) and 67/121 (55.4%) achieved functional remission, respectively. By the 3-year OLE endpoint, the rates of symptomatic remission (PP3M/PP6M:43/53 [81.1%]; PP6M/PP6M:87/101 [86.1%]) and functional remission (PP3M/PP6M:31/53 [58.5%]; PP6M/PP6M:60/102 [58.8%]) were sustained in both treatment groups. In addition, >56% of patients who transitioned from PP3M to PP6M or continued PP6M treatment had sustained combined (symptomatic and functional) remission at the OLE endpoint.

Conclusion: These findings support the long-term efficacy of PP3M and PP6M, highlighting the potential benefits of transitioning to longer acting antipsychotic formulations in achieving and sustaining both symptomatic stability and functional improvement in adults with schizophrenia.

Keywords: functional remission, long-acting injectable antipsychotics, paliperidone palmitate 6-month, schizophrenia, symptomatic remission

Introduction

Remission is a critical treatment outcome in the long-term management of schizophrenia. Broadly, it encompasses attenuation of core psychotic symptoms (symptomatic remission) and improvements in social, occupational and daily functioning (functional remission).[1,2] Together, symptomatic and functional remission reflects symptom stability, and better outcomes in humanistic aspects of a patient's life such as independent living, employability, self-care and social re-integration, all of which are central to recovery-oriented care.[3–5] Symptomatic remission, as defined by the Andreasen criteria (Remission in

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Schizophrenia Working Group [RSWG]), has helped establish a clearly identifiable outcome.[6] Functional remission, on the other hand, is multidimensional, lacks a standardized definition and is often difficult to achieve and measure, even in patients who achieve symptomatic remission.[2,7–9]

Several factors, including early intervention and improvements in disease symptoms and severity, treatment adherence, and psychosocial rehabilitation, are associated with higher rates of remission.[2,3,10] Predictors of remission also include patient-specific characteristics, such as early stages of illness and absence of severe negative symptoms, as well as the type of antipsychotic therapy used.[2,10] Adherence to antipsychotic treatment plays a crucial role in achieving and maintaining remission in schizophrenia.[11,12] The likelihood of achieving remission decreases with each relapse, with studies showing that around 17% of patients fail to remit after each psychotic episode, regardless of the episode number.[13] Therefore, long-term maintenance of treatment effects and relapse prevention are essential for sustaining remission. Across different study settings, the use of long-acting injectable (LAI) antipsychotics has shown to significantly ($p < 0.05$) reduce the risk of hospitalization or relapse by 8% to 12% versus oral antipsychotics.[14] Furthermore, early improvement in psychiatric symptoms with LAI antipsychotics has also been reported to predict subsequent improvements in functioning and psychosocial remission in patients with schizophrenia.[10,15]

The three available LAI formulations of paliperidone palmitate (PP) – once monthly (PP1M), three-monthly (PP3M), and six-monthly (PP6M) – provide treatment options for advancing patient-centered care in the management of adult patients with schizophrenia.[16–18] Supporting the efficacy data for delayed time to relapse, lower relapse rates, and reduced hospitalization, >50% of patients treated with PP1M and PP3M reached symptomatic remission during the last 6 months of a double-blind (DB) treatment phase (PP1M: 50.8%; PP3M: 50.3%). Similar functional (PP1M: 43.9%; PP3M: 42.5%) and combined symptomatic/functional remission rates (PP1M: 26.6%; PP3M: 25.1%) were also observed between treatment groups.[19,20] The PP6M formulation has expanded the range of PP LAIs, allowing for only two doses per year and has demonstrated noninferior efficacy to PP3M in preventing relapses (relapse-free rates at 12 months: PP6M, 92.5% vs PP3M, 95%).[18] Continued treatment with PP6M for up to three years has been shown to provide prolonged relapse prevention (relapse free rate: 95.9%) without raising any new safety concerns.[21] However, data on symptomatic and functional remission with PP6M over a 3-year period are currently unavailable and would be of clinical importance to further support treatment decision in the long-term management of schizophrenia.

The aim of this post-hoc analysis was to evaluate symptomatic and functional remission with PP6M treatment in order to assess its long-term efficacy in the management of schizophrenia. The analyses involved an assessment of symptomatic and functional remission rates over a 3-year period in patients who transitioned from PP3M to PP6M (PP3M/PP6M) or continued PP6M (PP6M/PP6M) from a 1-year DB noninferiority trial[18] through a 2-year open-label extension (OLE) study.[22]

Methods

Study Design and Patients

This post-hoc analysis was based on data from two studies of PP6M (Figure 1). The full methodology of the DB, randomized, active-controlled, parallel-group multicenter noninferiority trial (NCT03345342)[18] and the single-arm OLE study (NCT04072575)[22] have been published previously.

Patients (aged 18 to 70 years) diagnosed with schizophrenia (based on criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition [DSM-5]) at least 6 months before screening with a Positive and Negative Syndrome Scale (PANSS) total score <70 at screening were enrolled in the noninferiority study. Major exclusion criteria included primary, active DSM-5 diagnosis other than schizophrenia, attempted suicide within a year before screening or at imminent risk suicidal behavior, moderate-to-severe substance abuse (DSM-5 criteria) within 6 months of screening and receiving involuntary psychiatric treatment.

The noninferiority trial comprised a 28-day screening phase, an open-label transition phase, followed by a 1- or 3-month open-label maintenance phase with PP1M (156 or 234 mg) or PP3M (546 or 819 mg), respectively, and up to a 12-month DB phase, during which patients were randomized (2:1) to either PP3M (546 or 819 mg) or PP6M (1092 or 1560 mg). Eligible patients from six participating countries (Argentina, Hong Kong, Italy, Poland, the Russian

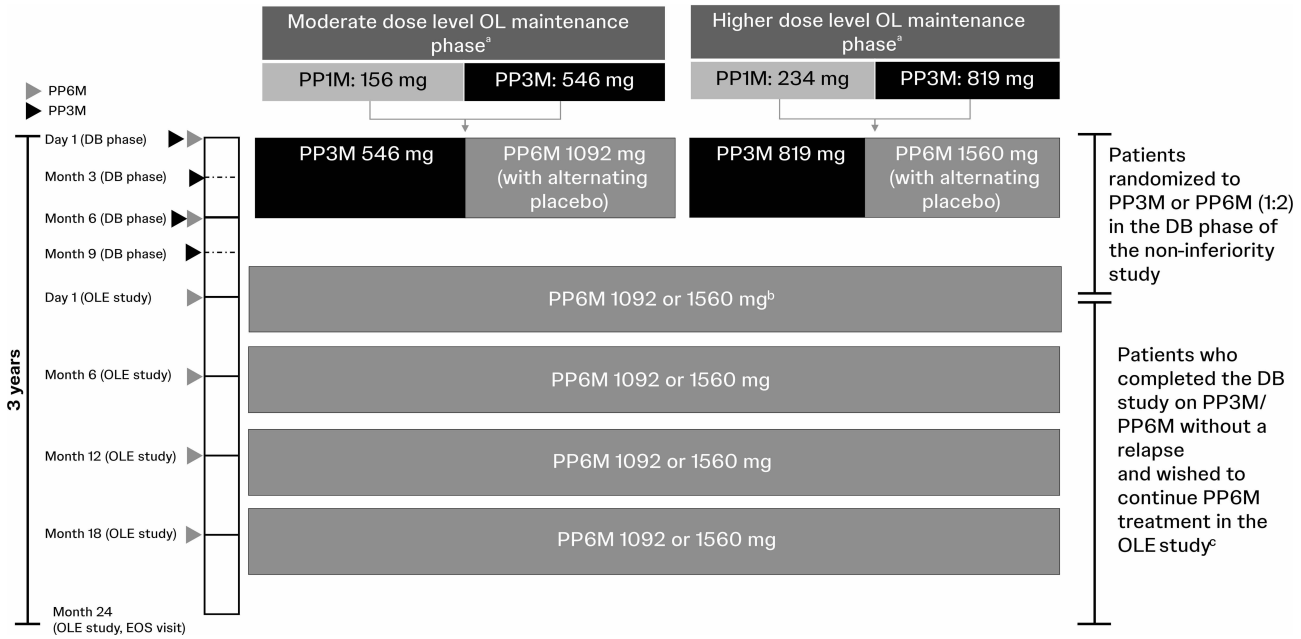

Figure 1 Study design. [a]Patients previously treated with oral antipsychotics, injectable risperidone microspheres, or a moderate or higher dose of PP1M but without previous stabilization (defined as ≥3 monthly injections, with the last 2 doses being the same dose strength) received additional doses of PP1M during a conditional OL transition phase. [b]The initial dose of PP6M in OLE study was determined based on the DB phase dose (moderate or higher). Flexible dosing was permitted at subsequent visits; however, due to the long-acting nature of PP6M, a dose change could take many months to become apparent. [c]The OLE study was limited to 6 participating countries (Argentina, Hong Kong, Italy, Poland, the Russian Federation, and Ukraine) and enrolment was optional.
Abbreviations: DB, double-blind; EOS, end of study; OL, open-label; OLE, open-label extension; PP1M, paliperidone palmitate 1-month formulation; PP3M, paliperidone palmitate 3-month formulation; PP6M, paliperidone palmitate 6-month formulation.

Federation, and Ukraine) who completed the noninferiority trial without relapse, had an option (at the patient's or investigator's discretion) to enroll into the 2-year OLE study. Patients received a total of 4 doses of PP6M (1092 or 1560 mg) at baseline, 6-month, 12-month, and 18-month visits.

Since this was a post-hoc analysis of previously published data, additional ethics committee or institutional review board approvals were not required. Independent ethics committee or the institutional review boards at each participating site approved the study protocols. The studies were conducted according to the principles of the Declaration of Helsinki and guidelines for Good Clinical Practice and applicable regulatory requirements. All patients provided written informed consent prior to study participation.

Assessments

In both studies, the severity of schizophrenia symptoms was assessed using the clinician-administered 30-item PANSS scale, which consists of 7 items measuring positive symptoms, 7 items assessing negative symptoms, and 16 items measuring general psychopathology. Each item is rated between 1 (no symptoms) to 7 (extreme symptoms), and a total scale score ranging from 30 to 210.[23] Symptomatic remission was assessed according to Andreasen's criteria and defined as a score of ≤3 on the following symptom score (PANSS) items: P1 (delusions), P2 (conceptual disorganization), P3 (hallucinatory behavior), N1 (blunted affect), N4 (social withdrawal), N6 (lack of spontaneity), G5 (mannerisms/ posturing), and G9 (unusual thought content) that is sustained for ≥6 months, with 1 excursion allowed.[6]

Functional remission was defined as a Personal and Social Performance (PSP) scale score >70 at all assessment time points, with no excursion allowed. The PSP is a 100-point single-item rating scale comprising four key domains: (1) socially useful activities such as work and study, (2) personal and social relationships (ie family, friends, partner etc.), (3) self-care such as hygiene, and (4) disturbing and aggressive behavior. A PSP total score between 71 and 100 (>70) indicates good functioning; a score between 31 and 70 indicates varying degrees of difficulty, and a score of ≤30 indicates poor functioning.[24,25]

Statistical Analyses

Symptomatic and functional remission analyses were conducted using the 3-year intent-to-treat (ITT) analysis set, defined as all patients who received ≥1 dose of study drug during the DB phase and the OLE study. The number and percentage of patients achieving remission (symptomatic, functional, or combined) at different post-baseline time points were presented by treatment group.

Results

Patients

Overall, 702 patients were treated with either PP3M (n = 224) or PP6M (n = 478) in the DB phase of the noninferiority trial; 571 completed the 12-month DB phase without a relapse, of which, 178 chose to continue treatment with PP6M and entered the OLE study. Thus, the post-hoc analysis included a total of 178 patients who either transitioned from PP3M in the DB phase of the noninferiority trial to PP6M in the 2-year OLE study (PP3M/PP6M, n = 57) or continued to receive PP6M (PP6M/PP6M, n = 121) from the noninferiority trial and the subsequent OLE study. The demographic and baseline characteristics of patients in the noninferiority and OLE studies have been described in detail previously.[18,22] The demographic and baseline characteristics were similar between the PP3M/PP6M and PP6M/PP6M cohorts in this post-hoc study (Table 1).

Symptomatic Remission

At the end of 1 year, the DB endpoint, 47/57 (82.5%) PP3M/PP6M patients and 103/121 (85.1%) PP6M/PP6M patients achieved symptomatic remission (Figure 2). At the OLE endpoint, 43/53 (81.1%) PP3M/PP6M patients and 87/101 (86.1%) PP6M/PP6M patients maintained symptomatic remission.

Functional Remission

At the end of 1 year, the DB endpoint, 30/57 (52.6%) PP3M/PP6M patients and 67/121 (55.4%) PP6M/PP6M patients achieved functional remission. At the OLE endpoint, functional remission was maintained with observed increases over the 3-year period (31/53 [58.5%] PP3M/PP6M patients and 60/102 [58.8%] PP6M/PP6M) (Figure 3).

Over the 3-year study period, there were no patients in the poor (PSP < 30) category (Table 2). The number of patients in the variable (PSP > 30 to ≤ 70) category consistently decreased, while the number of patients in the good (PSP > 70) category increased over time, indicating an overall improvement in functioning.

Table 1 Demographics and Baseline Characteristics (PP6M 3-year ITT)

Characteristic	PP3M/PP6M (n=57)	PP6M/PP6M (n=121)
Age at NI study screening visit, years, mean (SD)	39.9 (9.69)	38.6 (11.24)
Sex, n (%)		
Women	14 (24.6)	38 (31.4)
Men	43 (75.4)	83 (68.6)
Baseline BMI at NI study (OL phase), mean (SD), kg/m^2	26.9 (5.14)	27.9 (4.84)
Age at first diagnosis of schizophrenia, years, mean (SD)	29.3 (8.73)	27.5 (9.21)
PANSS score, mean (SD)		
NI study baseline (DB)	53.1 (10.05)	53.4 (9.72)
OLE study baseline	50.2 (10.77)	49.4 (10.40)
PSP score, mean (SD)		
NI study baseline (DB)	69.8 (11.69)	68.7 (12.10)
OLE study baseline	71.5 (11.84)	71.5 (10.79)

Abbreviations: BMI, body mass index; DB, double-blind; ITT, intent-to-treat; NI, noninferiority; OL, open-label; OLE, open-label extension; PANSS, Positive and Negative Syndrome Scale; PP3M, paliperidone palmitate 3-month formulation; PP6M, paliperidone palmitate 6-month formulation; PSP, Personal and Social Performance scale; SD, standard deviation.

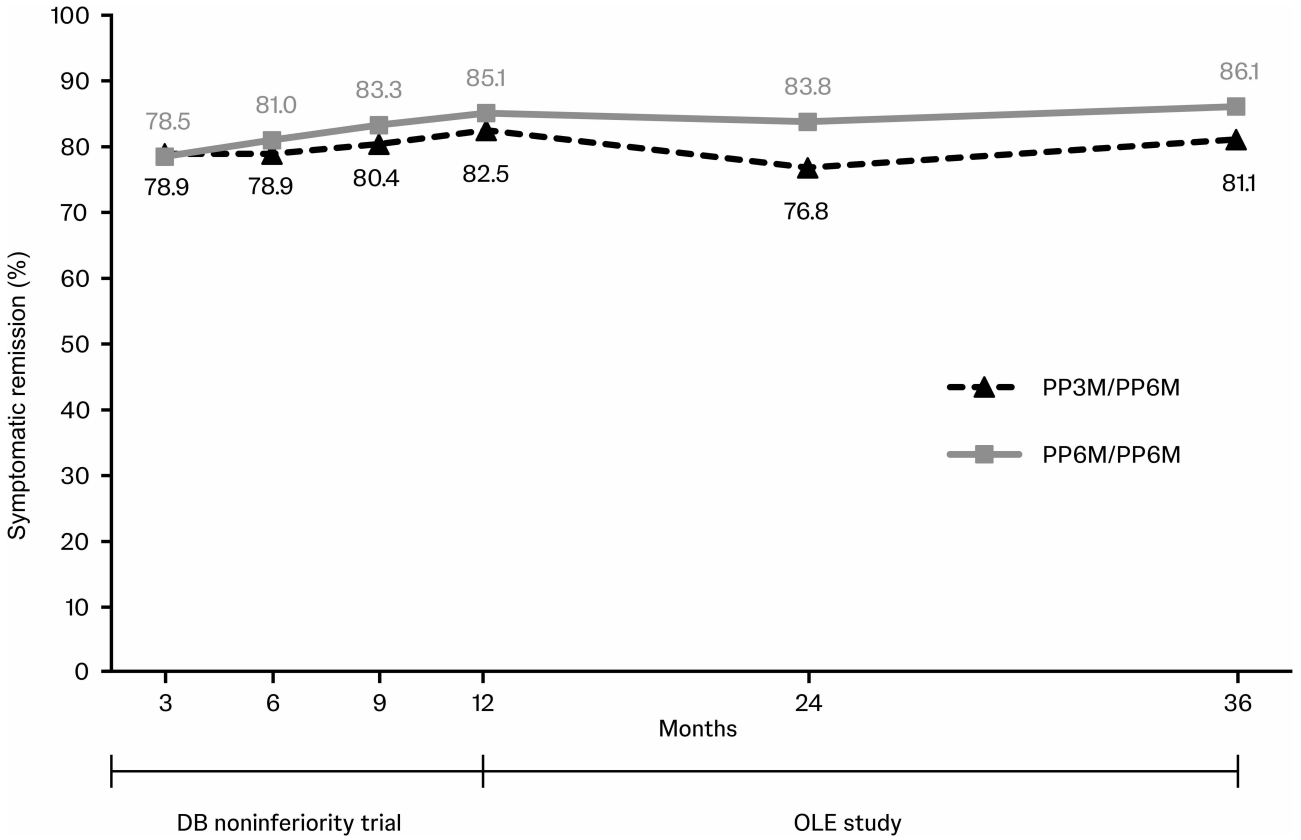

Figure 2 Proportion of patients achieving symptomatic remission through the 3-year study period (ITT population).
Abbreviations: DB, double-blind; ITT, intent-to-treat; OLE, open-label extension; PP3M, paliperidone palmitate 3-month formulation; PP6M, paliperidone palmitate 6-month formulation.

Combined Remission

At the end of 1 year, the DB endpoint, 27/57 (47.4%) patients in the PP3M/PP6M group and 63/121 (52.1%) in the PP6M/PP6M group met the criteria for both symptomatic and functional remission. By the end of 3 years, at the OLE endpoint, 30/53 (56.6%) patients in the PP3M/PP6M group and 58/102 (56.9%) in the PP6M/PP6M group met the criteria for both symptomatic and functional remission (Figure 4). Notably, most patients who achieved combined remission at the DB endpoint maintained remission with rates steadily increasing throughout the 3-year period.

Discussion

In this 3-year post-hoc analysis, patients who transitioned from PP3M to PP6M or continued PP6M treatment for up to 3 years had sustained functional and symptomatic remission, suggesting the long-term efficacy of these treatments in adult patients with schizophrenia. Most patients who achieved combined symptomatic and functional remission at the DB endpoint maintained their status with steady improvement over the 3-year period. Over 56% of those transitioning from PP3M to PP6M or continuing PP6M achieved both symptomatic and functional remission at the 3-year timepoint. Sustained remission, as observed in this post-hoc analysis, is an important outcome of schizophrenia treatment for improved patient well-being and recovery, a concept that involves concurrent achievement of symptomatic and functional remission.[26] Therefore, identifying treatments that can provide long-term symptomatic and functional stability is key in effective clinical management of schizophrenia.[3,26]

Overall, the rates of symptomatic remission reported vary widely from 16% to 78%, with differences largely attributed to factors such as study design, patient population (higher rates seen in first-episode patients and lower rates in those with more chronic disease), and the remission definition used.[12,27] The rates of symptomatic remission (>80%) observed at the end of the DB treatment phase and the 3-year OLE study in this study were notably higher than those

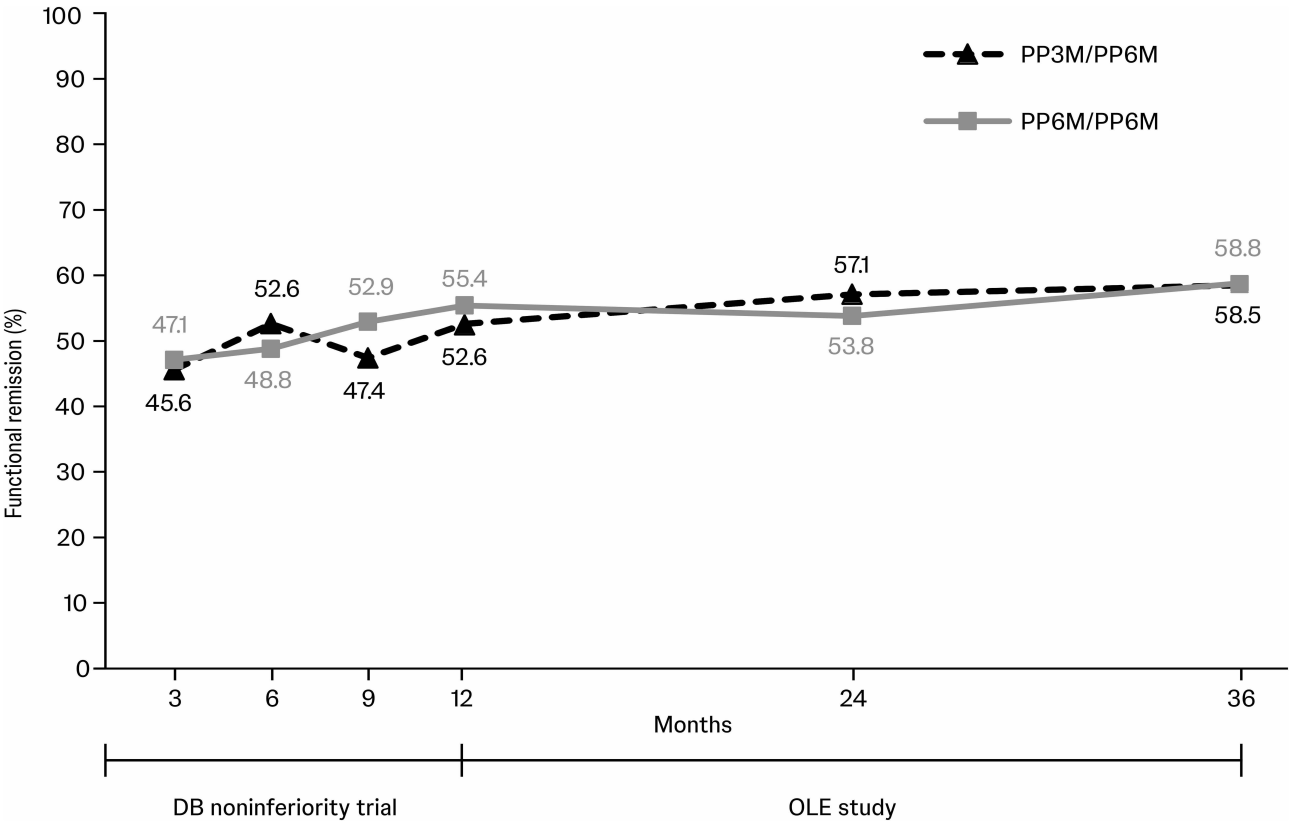

Figure 3 Proportion of patients achieving functional remission through the 3-year study period (ITT population).
Abbreviations: DB, double-blind; ITT, intent-to-treat; OLE, open-label extension; PP3M, paliperidone palmitate 3-month formulation; PP6M, paliperidone palmitate 6-month formulation.

reported in earlier studies using the same PANSS-based RSWG definition (45% to 60%) across different subpopulations and studies.[2,19,20,28–30] These findings underscore the efficacy of long-term PP LAI use, likely attributed to factors such as stable plasma levels of antipsychotic medication, improved adherence from reduced dosing frequency, and enhanced treatment continuity.[20,31]

Table 2 Shift in PSP Score from DB Baseline in Three Categories (Poor, Variable, Good); (PP6M 3-year ITT)

	PSP total score			
	Poor (≤30)	**Variable (>30 to ≤70)**	**Good (>70)**	**Total**
PP3M/PP6M				
Month 3 LOCF				
Poor (≤30)	0	0	0	0
Variable (>30 to ≤70)	0	29	2	31
Good (>70)	0	5	21	26
Total	0	34	23	57
Month 6 LOCF				
Poor (≤30)	0	0	0	0
Variable (>30 to ≤70)	0	26	1	27
Good (>70)	0	8	22	30
Total	0	34	23	57

(*Continued*)

Table 2 (Continued).

	PSP total score			
	Poor (≤30)	**Variable (>30 to ≤70)**	**Good (>70)**	**Total**
Month 9 LOCF				
Poor (≤30)	0	0	0	0
Variable (>30 to ≤70)	0	27	3	30
Good (>70)	0	7	20	27
Total	0	34	23	57
Month 12 LOCF				
Poor (≤30)	0	0	0	0
Variable (>30 to ≤70)	0	24	3	27
Good (>70)	0	10	20	30
Total	0	34	23	57
Month 24 LOCF				
Poor (≤30)	0	0	0	0
Variable (>30 to ≤70)	0	21	3	24
Good (>70)	0	12	20	32
Total	0	33	23	56
Month 36 LOCF				
Poor (≤30)	0	0	0	0
Variable (>30 to ≤70)	0	20	2	22
Good (>70)	0	13	21	34
Total	0	33	23	56
End Point				
Poor (≤30)	0	0	0	0
Variable (>30 to ≤70)	0	20	2	22
Good (>70)	0	13	21	34
Total	0	33	23	56
PP6M/PP6M				
Month 3 LOCF				
Poor (≤30)	0	0	0	0
Variable (>30 to ≤70)	0	58	6	64
Good (>70)	0	16	41	57
Total	0	74	47	121
Month 6 LOCF				
Poor (≤30)	0	0	0	0
Variable (>30 to ≤70)	0	54	8	62
Good (>70)	0	20	39	59
Total	0	74	47	121
Month 9 LOCF				
Poor (≤30)	0	0	0	0
Variable (>30 to ≤70)	0	54	3	57
Good (>70)	0	20	44	64
Total	0	74	47	121
Month 12 LOCF				
Poor (≤30)	0	0	0	0
Variable (>30 to ≤70)	0	52	2	54
Good (>70)	0	22	45	67
Total	0	74	47	121

(*Continued*)

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Table 2 (Continued).

	PSP total score			
	Poor (≤30)	**Variable (>30 to ≤70)**	**Good (>70)**	**Total**
Month 24 LOCF				
Poor (≤30)	0	0	0	0
Variable (>30 to ≤70)	0	49	5	54
Good (>70)	0	23	40	63
Total	0	72	45	117
Month 36 LOCF				
Poor (≤30)	0	0	0	0
Variable (>30 to ≤70)	0	47	5	52
Good (>70)	0	25	40	65
Total	0	72	45	117
End Point				
Poor (≤30)	0	0	0	0
Variable (>30 to ≤70)	0	47	5	52
Good (>70)	0	25	40	65
Total	0	72	45	117

Abbreviations: DB, double-blind; ITT, intent-to-treat; LOCF, last observation carried forward; PP3M, paliperidone palmitate 3-month formulation; PP6M, paliperidone palmitate 6-month formulation; PSP, Personal and Social Performance scale.

Consistent with the data for symptomatic remission, patients also achieved and maintained functional remission in both the PP3M/PP6M and PP6M/PP6M treatment groups and showed minimum clinically important difference (shift from moderate [>30 to ≤70] to mild impairment [>70] or mean PSP score change ≥7 points) in PSP categories from baseline.[25] The rates observed at the 1-year DB endpoint (>50%) and the 3-year OLE endpoint (>58%) were higher than the rates observed in previous studies (27% to 44%) reporting functional remission based on PSP score >70.[19,20] Functional remission, as part of the broader concept of recovery, emphasizes not only symptom control but also improvements in social functioning and quality of life, which are often difficult to achieve.[8,9,12] Functional outcome measures in schizophrenia are multidimensional and are commonly assessed using scales such as the Global Assessment of Functioning (GAF), PSP, and the Functional Remission of General Schizophrenia scale (FROG).[2,24,32,33] However, a consensus definition delineating functional remission as a clear outcome, which would facilitate meaningful comparisons across treatments, remains absent. Several studies have shown that patients in remission tend to have better functional outcomes than patients who did not achieve remission, highlighting the link between remission and improved functioning. However, only 30% to 38% of patients in remission meet stringent functional criteria, such as scoring above 80 on the GAF scale or fulfilling vocational and independent living criteria.[3,34] Studies show that while up to 50% of patients met the Andreasen remission criteria, only 17% to 20% met the more stringent criteria of holistic recovery and reached functional remission.[8,34,35] The findings from the current study demonstrate that a high proportion of patients achieved remission in psychosocial and other functional domains with continuous PP6M treatment. These results are clinically meaningful, with significant implications for improved daily functioning, social interactions, and potentially maximizing chances of recovery for patients with schizophrenia. Taken together, these findings on remission contribute to the growing body of evidence supporting the effectiveness of PP LAIs in reducing relapses and treatment failures in schizophrenia.[36] They underscore the importance of initiating treatment with appropriate antipsychotics to enhance dosing flexibility, medication adherence, and long-term outcomes in schizophrenia.

In this post-hoc analysis, the Andreasen criteria based on PANSS, and the PSP total score adequately captured both symptomatic and functional domains, offering a robust measure of comprehensive clinical remission using endpoints across the two studies. Longitudinal studies have consistently shown that patients in remission have significantly better symptom status over time than patients who do not achieve remission, with PANSS total score differences between 8 and

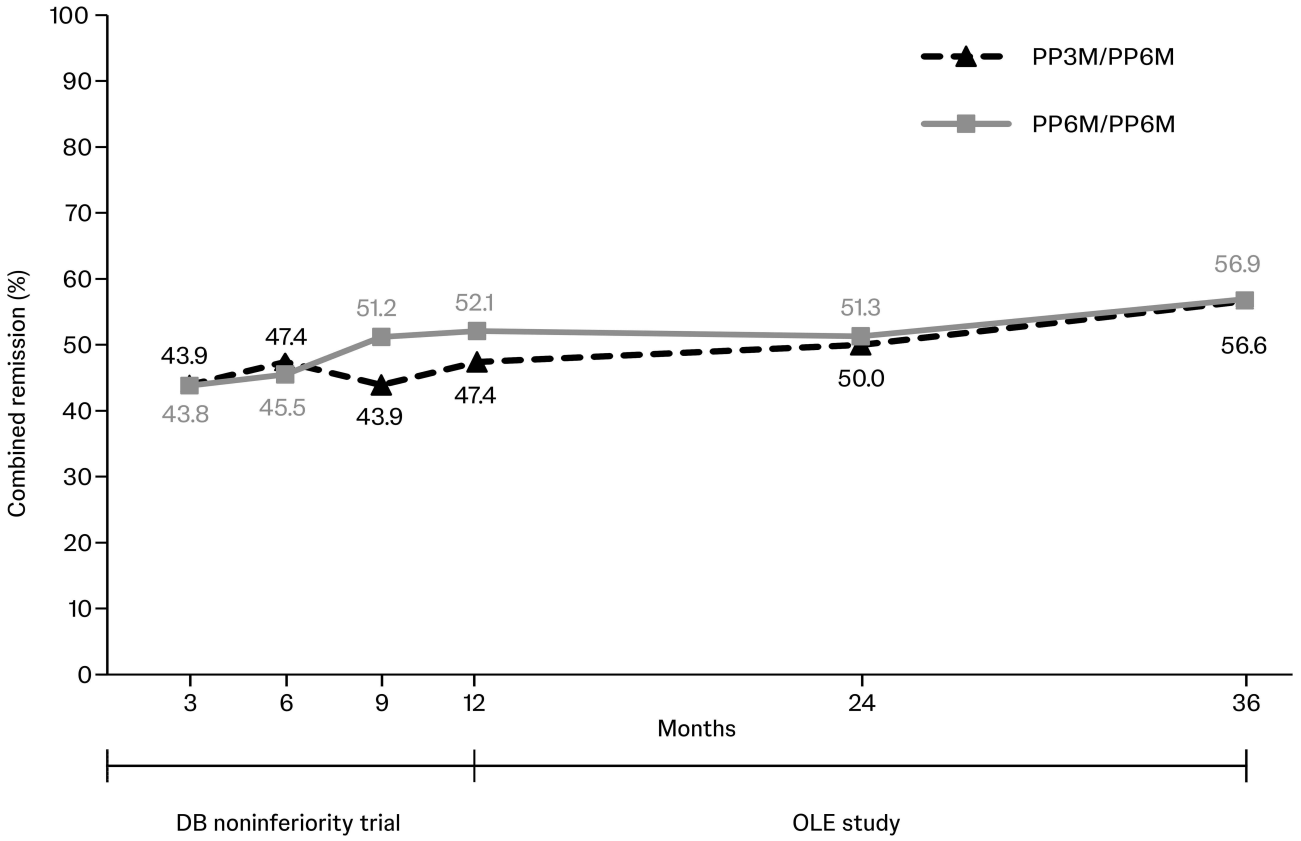

Figure 4 Proportion of patients achieving combined symptomatic and functional remission through the 3-year study period (ITT population).
Abbreviations: DB, double-blind; ITT, intent-to-treat; OLE, open-label extension; PP3M, paliperidone palmitate 3-month formulation; PP6M, paliperidone palmitate 6-month formulation.

25 points at follow-up and a mean PANSS score of 47, indicating low psychopathology.[12] Furthermore, a validation study reported the accuracy of the Andreasen's criteria, with 85% specificity and 75% sensitivity, confirming its usefulness as an indicator of overall symptomatic status in schizophrenia.[37] Achieving functional remission, defined as a PSP score >70, has been correlated with improvements in PANSS negative score, disease severity (CGI-S score) and treatment satisfaction.[4,38,39] A PSP score of >70 has also been associated with improvements in other measures of schizophrenia such as the Extrapyramidal Symptoms Rating Scale (ESRS) total score, improved overall mental and physical health (as measured using 36-item Short Form Survey [SF-36]), improved sleep quality and lower caregiver burden.[4,39] These findings support the utility of the PSP scale as a measure of multiple functional domains and outcomes that have clinically relevant impact on patients with schizophrenia.

These analyses are subject to limitations including the post-hoc nature of the analysis and lack of a comparator group. The criteria of clinical stability before entry into the DB phase in the noninferiority study may limit the generalizability of these findings to the broader real-world clinical population. However, this criterion was essential to the study design, as PP6M is not intended for use in acutely ill patients with schizophrenia. Additionally, only relapse-free patients who completed the DB treatment phase and voluntarily entered the OLE phase were included in the study. Thus, these patients may have improved adherence and better outcomes compared to patients who relapsed or withdrew after the DB phase. Furthermore, patients at imminent risk of suicide or violent behavior, and with moderate or severe substance use disorder or other clinically significant co-morbidities were excluded from the noninferiority study, making the sample less representative of the broader target population of patients with schizophrenia. Thus, assessment of remission data for PP6M from more pragmatic clinical trials and real-world samples is warranted to improve the generalizability of these findings, and inform more effective, patient-centered strategies.

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Conclusions

The current analyses provide long-term, longitudinal data over a period of 3 years demonstrating the efficacy of PP3M and PP6M LAIs in maintaining stable, long-term symptomatic and functional remission in patients with schizophrenia. Findings suggest that symptomatic and functional remission are achievable outcomes in a considerable proportion of patients receiving PP6M or transitioning from PP3M to PP6M over a 3-year period. With its half-yearly dosing window, PP6M broadens the range of maintenance treatment options and may help reduce the burden of frequent dosing, support adherence, and facilitate long-term treatment planning in routine clinical practice. These results reinforce the role of LAIs in promoting sustained remission and potential recovery in adult patients with schizophrenia.

Data Sharing Statement

The data sharing policy of Johnson & Johnson is available at https://innovativemedicine.jnj.com/our-innovation/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.

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Author Contributions

All authors made a significant contribution to the work reported, whether in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

JH is a psychiatric nurse practitioner and is a consulting speaker for Tempus AI, Inc., a consultant for the Point of Care Network, and a consultant for Johnson & Johnson. KLJ, JS, IT, LL and CO are employees of Johnson & Johnson, USA. JA is an employee of Johnson & Johnson, Portugal and holds company stocks or stock options. GM serves as a consultant for AbbVie, Alkermes, Alfasigma, Ironshore, Janssen, Lundbeck, Major League Baseball, Otsuka, National Football League, Neos, NLS Pharma, Purdue, Rhodes, Sage Therapeutics, Inc., Sunovion, Supernus, Takeda, Teva, and Vanda and as a speaker for AbbVie, Alkermes, Ironshore, Janssen, Lundbeck, Otsuka, Neos, Shire, Sunovion, Takeda, Teva, and personal fees from Johnson and Johnson. The authors report no other conflicts of interest in this work.

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