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Patient Satisfaction with 6-Monthly Versus 3-Monthly Paliperidone Palmitate Long-Acting Injectable for Schizophrenia Treatment: Results from a Phase-3, Randomised, Noninferiority Study

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INTRODUCTION

- Patient satisfaction with antipsychotic treatments for schizophrenia is a key predictor of treatment adherence, success, and quality of life.[1-3]
- Patients' satisfaction and preference generally increases with long-acting injectables (LAI) compared to oral antipsychotic treatments.[4]
- Current LAI antipsychotic treatments can be administered every two weeks to every three months and LAIs with longer dosing intervals help to ensure treatment continuity, especially in patients with limited access to healthcare or medication adherence issues.
- Paliperidone palmitate 6-monthly (PP6M) formulation LAI has a substantially longer dosing interval of six months, enabling just two injections per year, and received FDA and EMA approval in 2021.

OBJECTIVES

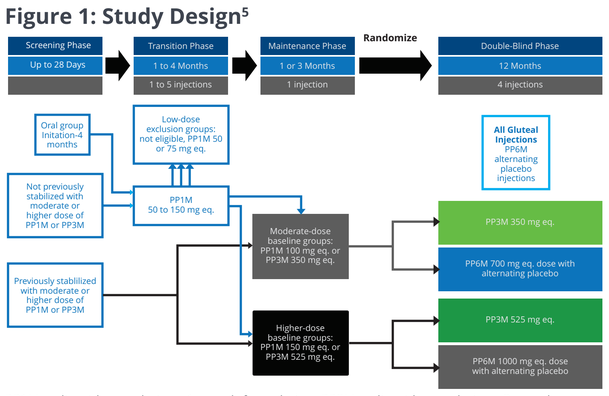
- To assess patient satisfaction with their treatment and social roles with PP6M and PP 3-monthly (PP3M) in a double-blind (DB), randomised study conducted in adult patients with schizophrenia transitioning from oral treatment.

METHODS

Study Overview

- Phase 3, double-blind (DB), randomised, active-controlled, parallel-group multicentre study (NCT03345342) conducted in 20 countries globally.[5]
- Eligible patients (aged 18-70 years) had DSM-5 diagnosis of schizophrenia for ≥6 months before screening and had a Positive and Negative Syndrome Scale (PANSS) total score of <70 points at screening. Patients were receiving treatment with PP 1-monthly (PP1M [100 mg eq./150 mg eq.]) or PP3M (350 mg eq./525 mg eq.), injectable risperidone microspheres, or any oral antipsychotic (except clozapine).
- Following a screening phase (up to 28 days), patients previously stabilised on PP1M (for ≥3 months) or PP3M (for at least one 3-month injection cycle) entered an open-label (OL)-maintenance phase (MA) and received 1 injection cycle of PP1M (100 mg eq./150 mg eq.) or PP3M (350 mg eq./525 mg eq.) **(Figure 1)**.
- Patients not stabilised on PP1M/PP3M underwent stabilisation for 1-4 months on PP1M during an OL-transition phase.
- After maintenance phase, clinically stable patients were randomised (2:1) to PP6M (700 mg eq./1000 mg. eq.) or PP3M (350 mg eq./525 mg eq.) as dorsogluteal injections in a 12-month DB phase. Doses were fixed throughout the DB phase. Doses in the DB phase corresponded to the prescribed doses of PP1M and PP3M in previous phases.

Figure 1: Study Design[5]



PP1M, paliperidone palmitate 1-month formulation; PP3M, paliperidone palmitate 3-month formulation; PP6M, paliperidone palmitate 6-month formulation.

Assessments

- Patient satisfaction with treatment and with participation in social roles were measured using the following scales:
  - Patient-Reported Outcomes Measurement Information System (PROMIS) Satisfaction with Participation in Social Roles (SPSR)[6]:
    - PROMIS SPSR Short Form 8a assessed patients' satisfaction with participation in social roles, such as work, marital, and family responsibilities.
    - Patients were asked to consider the previous 7 days and to rate 8 items on 5-point Likert scale, with higher scores representing higher satisfaction.
  - Abbreviated Treatment Satisfaction Questionnaire for Medication (TSQM-9)[7]:
    - Assessed patients' satisfaction with the medication and the domains of effectiveness, convenience, and overall satisfaction.
    - Items were scored on 5- or 7-point Likert scales, with higher scores indicating higher satisfaction. The recall period was "the last 2 to 3 weeks."
- The scales were only administered to those patients entering the study on an oral antipsychotic pre-treatment, excluding those who started the study on LAIs.

Statistical Analysis

- Descriptive statistics were provided for baseline, at each assessment time point during the DB phase, and at end point (DB; end of month 12).
- Change from baseline (DB) at each visit during the DB Phase was analyzed using an analysis of covariance model (ANCOVA) with factors for treatment and country and baseline score as a covariate.

NEUROPSYCHIATRY

RESULTS

- A total of 124 patients in the PP3M and 282 patients in the PP6M groups were administered the SPSR and TSQM-9 at baseline.
- At the end of 12 months, 67/124 patients (54.03%) in the PP3M group and 146/282 (51.77%) patients in the PP6M group completed the SPSR, while 121/124 (97.58%) patients in the PP3M group and 279/282 (98.94%) in the PP6M group completed TSQM 9.

SPSR

- From the MA phase baseline to the end of month 12 (DB phase), the improvement in satisfaction with social roles was 18% in the PP3M group and 20% in the PP6M group.
- At the end of the DB phase, the mean (standard deviation [SD]) change in SPSR total score relative to the baseline (MA) was 4.5 (7.91) for the PP3M group and 5.0 (8.01) for the PP6M group; **(Table 1)**.
- The mean (SD) change in SPSR from baseline (DB) to the end of DB phase was 0.9 (7.15) for the PP3M group and 0.6 (6.58) for the PP6M group.
- Patients who transitioned from oral antipsychotic treatments showed an improvement in SPSR. In both treatment groups this improvement for patients transitioning from oral treatments was comparable.

Table 1: Changes in SPSR Total Score from Baseline (DB/MA) to the end of 12 Months DB Phase (DB ITT Population*)

	Baseline (DB) to end of 12 months (DB)		Baseline (MA) to end of 12 months (DB)	
	PP3M (N=124)	PP6M (n=282)	PP3M (N=124)	PP6M (n=282)
Baseline				
N	73	169	70	156
Mean (SD)	27.6 (6.50)	28.5 (7.24)	24.0 (7.03)	24.1 (8.16)
Median (range)	27.0 (15, 40)	30.0 (8, 40)	23.0 (8, 40)	24.0 (8, 40)
Endpoint				
N	71	158	71	158
Mean (SD)	28.1 (6.71)	29.0 (6.89)	28.1 (6.71)	29.0 (6.89)
Median (range)	30.0 (16, 40)	30.0 (8, 40)	30.0 (16, 40)	30.0 (8, 40)
Change from baseline				
N	70	154	67	146
Mean (SD)	0.9 (7.15)	0.6 (6.58)	4.5 (7.91)	5.0 (8.01)
Median (range)	0.0 (−21, 22)	0.5 (−22, 18)	5.0 (−14, 24)	5.0 (−30, 24)

*Patients who entered study on an oral antipsychotic treatment.
DB, double-blind; ITT, intent-to-treat; MA, maintenance; PP3M, paliperidone palmitate 3-month formulation; PP6M, paliperidone palmitate 6-month formulation; SD, standard deviation; SPSR, Satisfaction with Participation in Social Roles.

TSQM-9

- Treatment satisfaction measured by the TSQM-9, improved slightly during the DB phase of the study in both treatment groups for patients transitioning from oral antipsychotic treatments to PP3M/PP6M **(Table 2)**.
  - The mean (SD) change in overall satisfaction from baseline (DB) to end of month 12 was: PP3M, 2.5 (19.29) and PP6M, 0.5 (20.02).
  - Similar findings were noted across the sub-domains for effectiveness (PP3M: 6.0 [21.18]; PP6M: 3.6 [19.49]) and convenience (PP3M: 3.4 [17.76]; PP6M: 1.1 [15.30]).

Table 2: Changes in TSQM-9 Scores from Baseline (DB) to the end of 12 Months DB Phase (DB ITT Population*)

	Overall Satisfaction		Effectiveness		Convenience	
	PP3M (N=124)	PP6M (n=282)	PP3M (N=124)	PP6M (n=282)	PP3M (N=124)	PP6M (n=282)
Baseline						
N	124	282	124	282	124	282
Mean (SD)	70.6 (16.17)	70.7 (18.06)	69.3 (17.01)	70.3 (17.52)	73.8 (16.38)	75.1 (16.47)
Median (range)	69.4 (29, 100)	69.4 (−1, 100)	66.7 (0, 100)	66.7 (0, 100)	72.2 (0, 100)	72.2 (0, 100)
Endpoint						
N	121	279	121	279	121	279
Mean (SD)	73.3 (22.32)	71.2 (21.67)	75.3 (18.81)	73.8 (18.83)	77.2 (17.26)	76.1 (16.22)
Median (range)	76.4 (−8, 100)	76.4 (−1, 100)	77.8 (17, 100)	72.2 (0, 100)	83.3 (22, 100)	77.8 (0, 100)
Change from baseline						
N	121	279	121	279	121	279
Mean (SD)	2.5 (19.29)	0.5 (20.02)	6.0 (21.18)	3.6 (19.49)	3.4 (17.76)	1.1 (15.30)
Median (range)	1.4 (−71, 47)	0.0 (−85, 49)	5.6 (−67, 83)	0.0 (−67, 89)	0.0 (−61,100)	0.0 (−78, 67)

*Patients who entered study on an oral antipsychotic treatment.
DB, double-blind; ITT, intent-to-treat; PP3M, paliperidone palmitate 3-month formulation; PP6M, paliperidone palmitate 6-month formulation; SD, standard deviation; TSQM-9, abbreviated 9-item Treatment Satisfaction Questionnaire for Medication.

- Patients transitioning from oral antipsychotic treatment to PP3M or PP6M reported greater improvement in treatment satisfaction ("overall satisfaction") at the end of the DB phase compared to baseline (MA) **(Table 3)**.
  - PP3M: 32% and PP6M: 40%. The mean (SD) change was 21.4 (25.84) for the PP3M group and 17.2 (27.06) for the PP6M group.
  - Similar findings were noted across the sub-domains for effectiveness (PP3M: 18.5 [23.22]; PP6M: 15.4 [23.29]) and convenience (PP3M: 21.7 [23.46]; PP6M: 18.8 [22.84]).
  - Patients who switched from oral antipsychotic treatments to PP3M/PP6M reported higher levels of treatment satisfaction. This improvement for patients transitioning from oral treatments was comparable in both treatment groups.

Table 3: Changes in TSQM-9 Scores from Baseline (MA) to the end of 12 Months DB Phase (DB ITT Population*)

	Overall Satisfaction		Effectiveness		Convenience	
	PP3M (N=124)	PP6M (n=282)	PP3M (N=124)	PP6M (n=282)	PP3M (N=124)	PP6M (n=282)
Baseline						
N	124	282	124	282	124	282
Mean (SD)	52.3 (18.02)	54.0 (21.29)	57.0 (16.03)	58.3 (16.88)	56.0 (16.92)	57.6 (17.81)
Median (range)	49.3 (14, 100)	52.8 (−8, 100)	55.6 (0, 100)	55.6 (0, 100)	55.6 (17, 100)	55.6 (0, 100)
Endpoint						
N	121	279	121	279	121	279
Mean (SD)	73.3 (22.32)	71.2 (21.67)	75.3 (18.81)	73.8 (18.83)	77.2 (17.26)	76.1 (16.22)
Median (range)	76.4 (−8, 100)	76.4 (−1, 100)	77.8 (17, 100)	72.2 (0, 100)	83.3 (22, 100)	77.8 (0, 100)
Change from baseline						
N	121	279	121	279	121	279
Mean (SD)	21.4 (25.84)	17.2 (27.06)	18.5 (23.22)	15.4 (23.29)	21.7 (23.46)	18.8 (22.84)
Median (range)	22.2 (−61, 86)	22.2 (−78, 92)	16.7 (−50, 72)	16.7 (−67, 78)	22.2 (−44, 78)	16.7 (−72, 67)

*Patients who entered study on an oral antipsychotic treatment.
DB, double-blind; ITT, intent-to-treat; MA, maintenance; PP3M, paliperidone palmitate 3-month formulation; PP6M, paliperidone palmitate 6-month formulation; SD, standard deviation; TSQM-9, abbreviated 9-item Treatment Satisfaction Questionnaire for Medication.

CONCLUSIONS

Patients switching from oral antipsychotic treatments to LAIs (PP3M and PP6M) showed sustained improvement in measures of treatment satisfaction and satisfaction with their social roles.

Treatment satisfaction ("Overall Satisfaction") showed the largest improvement from baseline MA to the end of month 12 in both treatment arms with only a minor incremental improvement during the DB phase. Similar findings were noted across the sub-domains for "effectiveness" and "convenience."

The findings of this analysis provide patient-relevant information reinforcing the benefits of LAIs for schizophrenia treatment, specifically for patients who are switched from oral antipsychotic treatments to LAI formulations.

Limitations

- For TSQM-9, treatment with placebo injections in PP6M group during the DB phase may have impacted treatment satisfaction assessment.
- This study was not powered to show differences in treatment satisfaction between treatment arms.

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DISCLOSURES

RM, PD, PS, HR, AK and SW are employees of Janssen Research & Development, LLC and may hold stocks in Johnson & Johnson. SG was employed by Janssen Research & Development, LLC during the time the study was conducted and owns stock/stock options in Johnson & Johnson.
JMPT reports no conflicts of interest.

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