Treatment Satisfaction, Quality of Life, Satisfaction with Participation in Social Roles, and Caregiver Burden in Adults with Schizophrenia Treated with Paliperidone Palmitate Long-Acting Injectables

AUTHORS: Franklin Cline,[1] Elhussein Ibrahim,[2] Jordy Mehawej,[2] John Han,[2] R. Karl Knight,[2] Karen Johnston,[2] Mohamed Wahba,[3] Leslie Citrome[4,5]

AFFILIATIONS: [1]Sac Med, Inc., California, USA; [2]Johnson & Johnson, Titusville, New Jersey, USA; [3]Johnson & Johnson, Cairo, Egypt; [4]New York Medical College, Valhalla, New York, USA; [5]Feinberg School of Medicine, Chicago, Illinois, USA

Background

- Paliperidone palmitate 3-month (PP3M) and 6-month (PP6M) are long-acting injectable (LAI) antipsychotics with established efficacy and safety in the treatment of adults with schizophrenia.[1-4]
- While extensive evidence exists on the efficacy and safety of LAI antipsychotics in preventing relapse, less is known about their impact on patient-reported outcomes and caregiver burden.
- Patient-reported quality of life (QoL), treatment satisfaction, satisfaction with participation in social roles, and caregiver burden are important, yet underrepresented outcomes in schizophrenia clinical trials.

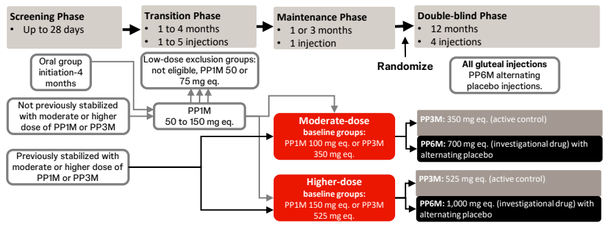
Objective

- This study of adults with schizophrenia, treated with the PP3M or PP6M formulations over 1 year, was conducted to determine overall treatment satisfaction, QoL, and satisfaction with participation in social roles, along with caregiver reported outcomes. (Data were derived from NCT03345342).

Methods

- Data from a 12-month, double-blind (DB), Phase 3, noninferiority study that compared PP6M with PP3M in adults with schizophrenia were analyzed.
- Men and women between 18 and 70 years of age who met the DSM-5 criteria of schizophrenia for ≥6 months before screening and had a full PANSS total score of <70 points at screening were eligible for enrollment.
- After screening, open-label transition, and maintenance (MA) phases, clinically stable participants who received moderate or higher doses of PP1M or PP3M were randomized (2:1; n=702) to PP6M (n=478) or PP3M (n=224) during the DB phase (**Figure 1**). This phase was designed to include ≥2 injections of PP6M (investigational drug with alternating placebo) or 4 injections of PP3M (active control).
- The patient-reported outcomes were assessed using the Schizophrenia Quality of Life Scale Revision 4 (SQLS-R4), Treatment Satisfaction Questionnaire for Medication 9-item version (TSQM-9), and the Patient-Reported Outcomes Measurement Information System (PROMIS) Satisfaction With Participation in Social Roles Short Form 8a (SPSR).
- Caregiver burden was assessed using the Involvement Evaluation Questionnaire (IEQ).

FIGURE 1: Study Design



Results

- During the DB phase, the percentage of participants who completed the study was similar in the PP3M and PP6M groups (202/224 [90.2%] and 416/478 [87.0%], respectively).
- Baseline SQLS-R4 was administered to 224 participants in the PP3M and 478 participants in the PP6M groups; at the end of 12 months, 219/224 participants (97.77%) in the PP3M group and 472/478 (98.74%) in the PP6M group completed the SQLS-R4.
- Baseline SPSR and TSQM-9 were administered to 124 participants in the PP3M and 282 participants in the PP6M groups; at the end of 12 months, 67/124 participants (54.03%) in the PP3M group and 146/282 (51.77%) in the PP6M group completed the SPSR, while 121/124 (97.58%) in the PP3M group and 279/282 (98.94%) in the PP6M group completed the TSQM-9.
- Baseline IEQ was provided to 163 caregivers in the PP3M and 325 caregivers in the PP6M groups; at the end of 12 months, 136/163 caregivers (83.44%) in the PP3M group and 273/325 (84.00%) in the PP6M group completed the IEQ.

SQLS-R4

- The SQLS-R4 assessed the effectiveness of treatment on schizophrenia-related QOL. The assessment was developed using items generated from in-depth patient interviews (ie, from the perspective of patients) and has 33 self-reported items in 2 subscales, psychosocial feelings and vitality/cognition. Higher scores indicate poorer QoL.[5]
- At Month 12, the SQLS-R4 total score improved by a median (interquartile range [IQR]) of 23.8% (-15.2% to 52.5%) with PP3M and 29.7% (-6.8% to 56.5%) with PP6M.
- Participants, who were previously on PP1M/PP3M, risperidone LAI, or transitioning from oral antipsychotics, reported improvement in QoL at Month 12 compared with baseline. The improvements were comparable between the 2 treatment groups (**Table 1**).

Table 1. Changes in SQLS-R4 Total Score from Baseline (DB/MA) to 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	PP6M	PP3M	PP6M
Baseline				
N	224	478	224	477
Mean (SD)	26.7 (15.47)	24.8 (15.02)	30.4 (16.21)	29.4 (15.38)
Median (range)	25.0 (0, 81)	23.9 (0, 73)	30.3 (1, 86)	28.8 (0, 78)
Endpoint				
N	219	473	219	473
Mean (SD)	25.3 (17.39)	23.3 (15.41)	25.3 (17.39)	23.3 (15.41)
Median (range)	22.0 (0, 76)	22.0 (0, 86)	22.0 (0. 76)	22.0 (0, 86)
Change from baseline				
N	219	473	219	472
Mean (SD)	-1.3 (12.5)	-1.3 (12.7)	-5.1 (15.53)	-6.1 (15.93)
Median (range)	-0.8 (-40, 46)	-2.3 (-37, 49)	-6.1 (-65, 48)	-5.3 (-55, 42)

Note: Descriptive statistics provided for baseline, endpoint, and change from baseline (based on LOCF data).
DB=double blind; ITT=intent-to-treat; LOCF=last observation carried forward; MA=maintenance; PP3M=paliperidone palmitate 3-month formulation; PP6M=paliperidone palmitate 6-month formulation; SD=standard deviation; SQLS-R4=Schizophrenia Quality of Life Scale Revision 4.

TSQM-9

- The TSQM-9 is a reliable and valid measure for assessing treatment satisfaction in naturalistic study designs,[6] with higher scores representing higher satisfaction.
- At Month 12, the TSQM-9 overall satisfaction improved by a median (IQR) of 51.5% (15.2% to 85.2%) with PP3M and 40.0% (0.0% to 89.5%) with PP6M.
- Participants transitioning from oral antipsychotics to PP3M or PP6M reported improved overall satisfaction at Month 12 compared with baseline (MA), and the improvements were comparable between the treatments (**Table 2a**). Similar findings were noted across sub-domains for effectiveness and convenience.
- Small incremental improvements in treatment satisfaction were observed from the baseline (DB) phase to the end of Month 12 in participants transitioning from oral antipsychotics to PP3M/PP6M (**Table 2b**).

Table 2a. Changes in TSQM-9 from Baseline (MA) to End of 12 Months DB Phase for Participants who Entered the Study on Oral Antipsychotics (DB ITT Population)

	Baseline (MA) to End of 12 Months (DB)					
	Overall Satisfaction		Effectiveness		Convenience	
	PP3M	PP6M	PP3M	PP6M	PP3M	PP6M
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)

Note: Descriptive statistics provided for baseline, endpoint, and change from baseline (based on LOCF data).
DB=double blind; ITT=intent-to-treat; LOCF=last observation carried forward; MA=maintenance; PP3M=paliperidone palmitate 3-month formulation; PP6M=paliperidone palmitate 6-month formulation; SD=standard deviation; TSQM-9=Treatment Satisfaction Questionnaire for Medication 9-item version.

Table 2b. Changes in TSQM-9 from Baseline (DB) to End of 12 Months DB Phase for Participants who Entered the Study on Oral Antipsychotics (DB ITT Population)

	Baseline (DB) to End of 12 Months (DB)					
	Overall Satisfaction		Effectiveness		Convenience	
	PP3M	PP6M	PP3M	PP6M	PP3M	PP6M
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)

Note: Descriptive statistics provided for baseline, endpoint, and change from baseline (based on LOCF data).
DB=double blind; ITT=intent-to-treat; LOCF=last observation carried forward; PP3M=paliperidone palmitate 3-month formulation; PP6M=paliperidone palmitate 6-month formulation; SD=standard deviation; TSQM-9=Treatment Satisfaction Questionnaire for Medication 9-item version.

SPSR

- The SPSR evaluates satisfaction with participation in social roles and was developed by the PROMIS group.[7] Participants were asked to consider the past 7 days and to rate 8 items related to satisfaction, with higher scores representing higher satisfaction.
- At Month 12, the SPSR scores increased by a median (IQR) of 21.1% (1.7% to 49.1%) with PP3M and 26.7% (3.2% to 58.8%) with PP6M.
- Participants transitioning from oral antipsychotics to PP3M or PP6M reported improvement in satisfaction with social roles at Month 12 compared with baseline. The improvements were comparable between the 2 treatment groups (**Table 3**).

Table 3. Changes in SPSR Total Score from Baseline (DB/MA) to End of 12 Months DB Phase for Participants who Entered the Study on Oral Antipsychotics (DB ITT Population)

	Baseline (DB) to End of 12 Months (DB)		Baseline (MA) to End of 12 Months (DB)	
	PP3M	PP6M	PP3M	PP6M
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)

Note: Descriptive statistics provided for baseline, endpoint, and change from baseline (based on LOCF data).
DB=double blind; ITT=intent-to-treat; LOCF=last observation carried forward; MA=maintenance; PP3M=paliperidone palmitate 3-month formulation; PP6M=paliperidone palmitate 6-month formulation; SD=standard deviation; SPSR=Satisfaction With Participation in Social Roles Short Form 8a.

IEQ

- The IEQ measured levels of caregiver consequences among family members and friends of participants with schizophrenia.[8] The assessment was completed by a designated caregiver (if available) and the 31 questions that comprise it were developed to evaluate caregiver burden across 4 dimensions (tension, supervision, worrying, and urging).[9]
- At Month 12, the IEQ score decreased by a median (IQR) of 37.5% (5.9% to 61.5%) with PP3M and 35.3% (9.1% to 60.9%) with PP6M.
- Caregivers reported overall reduced burden (sum-score) at Month 12 compared with baseline. Reductions in caregiver burden were comparable between the 2 treatment groups (**Table 4**).

Table 4. Changes in IEQ Sum-Score from Baseline (DB/MA) to 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	PP6M	PP3M	PP6M
Baseline				
N	163	325	157	316
Mean (SD)	19.5 (12.16)	18.5 (12.47)	23.1 (14.15)	23.4 (14.49)
Median (range)	16.0 (1, 63)	15.0 (0, 64)	19.0 (1, 60)	21.0 (0, 81)
Endpoint				
N	143	295	143	295
Mean (SD)	16.1 (12.96)	16.7 (12.70)	16.1 (12.96)	16.7 (12.70)
Median (range)	12.0 (0, 66)	14.0 (0, 62)	12.0 (0, 66)	14.0 (0, 62)
Change from baseline				
N	141	280	136	273
Mean (SD)	-2.7 (12.78)	-1.3 (9.80)	-6.4 (13.21)	-6.5 (13.29)
Median (range)	-2.0 (-51, 39)	-1.0 (-42, 46)	-6.0 (-39, 38)	-6.0 (-63, 46)

Note: Descriptive statistics provided for baseline, endpoint, and change from baseline (based on LOCF data).
DB=double blind; ITT=intent-to-treat; LOCF=last observation carried forward; MA=maintenance; PP3M=paliperidone palmitate 3-month formulation; PP6M=paliperidone palmitate 6-month formulation; SD=standard deviation; IEQ=Involvement Evaluation Questionnaire.

Key takeaway

PP3M and PP6M treatment over one year improved patient-reported outcomes and reduced caregiver burden.

Conclusions

- Participants treated with PP3M or PP6M for 12 months reported improvements in QoL, which were comparable between the treatments.
- Participants who entered the study on oral antipsychotics and transitioned to PP3M/PP6M for 12 months showed sustained improvements in treatment satisfaction and satisfaction with participation in social roles.
- Treatment satisfaction ("overall satisfaction") showed the largest improvement from baseline MA to the end of Month 12 with both PP3M and PP6M, with only minor incremental improvement during the DB phase. Similar findings were noted for the sub-domains of "effectiveness" and "convenience".
- Caregivers of participants who were treated with PP3M/PP6M reported clinically relevant reductions in caregiver burden.

Limitations

- Treatment with placebo injections in the PP6M group during the DB phase may have impacted treatment satisfaction assessment.
- The study was not powered to show differences in QoL, treatment satisfaction, satisfaction with participation in social roles, or caregiver burden between treatment arms.

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Disclosures

Jordy Mehawej, John Han, R. Karl Knight, Karen Johnston, and Mohamed Wahba are employees of Johnson & Johnson and may hold stocks/stock options in Johnson & Johnson. Elhussein Ibrahim is a Doctor of Pharmacy student at Temple University School of Pharmacy and was employed as an intern at Johnson & Johnson at the time of this publication. Franklin Cline serves on the speaker bureau for Johnson & Johnson as well as Luye Pharmaceuticals. Leslie Citrome reports no conflicts of interest.

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