Stable Schizophrenia Patients Switched to Paliperidone Palmitate 3-Monthly Formulation (PP3M) in Real Life: Functioning and Resource Use

Maria Paz Garcia-Portilla[1], Pierre-Michel Llorca[2], Giuseppe Maina[3], Vasilis P Bozikas[4], Halise Devrimci-Ozguven[5], Kim Sung Wan[6], Paul Bergmans[7], Irina Usankova[8], Pierre Cherubin[9], Katalin Pungor[10]

[1]University of Oviedo, CIBERSAM, Spain; [2]CMP B, CHU Clermont-Ferrand, Clermont Auvergne University, France; [3]SCDU Psichiatria, AOU San Luigi Gonzaga, Università degli Studi di Torino, Italy; [4]Second Department of Psychiatry, School of Medicine, Aristotle University of Thessaloniki, Greece; [5]Department of Psychiatry, School of Medicine, Ankara University, Turkey; [6]Chonnam National University Medical School, Gwangju, South Korea; [7]Janssen Cilag, Biostatistics & Programming, Breda, The Netherlands; [8]Johnson & Johnson, EMEA Medical Affairs Organization, Moscow, Russia; [9]Janssen Cilag, EMEA Medical Affairs, Issy-les-Moulineaux, France; [10]Janssen Cilag, EMEA Medical Affairs, Dusseldorf, Germany

INTRODUCTION

- In addition to improving clinical symptoms of schizophrenia, enhancing functioning is a key goal of antipsychotic therapy as this has a great impact on all areas of patients' lives, including quality of life and independence,[1,2] and healthcare resource utilization (HRU)[3, 4]
- Paliperidone 3-monthly formulation (PP3M) has demonstrated favourable efficacy and safety in clinically stable patients during randomized controlled trials (RCTs)[5-7]
  - In one RCT, >40% of patients receiving PP3M achieved functional remission (defined as a score of >70 on the Personal and Social Performance [PSP] scale)
  - However, due to the nature of these RCTs, only selected patient populations were included and real-world data on functional outcomes are lacking

OBJECTIVE

- To conduct a real-world study to assess the impact of conversion from paliperidone palmitate 1-month formulation (PP1M) to PP3M in a diverse population of patients with clinically stable schizophrenia
- The primary objective of this study was to assess symptomatic remission and secondary objectives included functioning, satisfaction with treatment and HRU
- This poster presents outcomes for the secondary objectives of the study

METHODS

Study design

- An international prospective Phase 3b, single-arm, non-randomized, open-label, 52-week study conducted in a diverse population of patients with schizophrenia seen in clinical practice (REMISSIO; ClinicalTrials.gov identifier NCT02713282)
- PP3M was administered from Day 1 to Day 360, with the last injection of PP3M at Month 9
- The initial dose of PP3M and subsequent dose changes (possible at clinicians' discretion) were made according to the product label[8]

Patients

- Patients aged 18–50 years with confirmed schizophrenia (*Diagnostic and Statistical Manual of Mental Disorders, 5th Edition*)
- Adequate treatment with PP1M for ≥4 months (the last two doses of PP1M being the same)
- A baseline Positive and Negative Syndrome Scale (PANSS) total score <70

Assessments

- Assessments were made at 3-monthly intervals during the treatment period
- A follow-up call for safety assessments was made at 3 months after Month 12 or study discontinuation

Outcomes

- Changes in PSP score, Subjective Wellbeing Under Neuroleptics (SWN-S) score, satisfaction with medication, assessment of daily activities, WHO Disability Assessment Schedule (WHODAS 2.0) score, and HRU
- The primary analysis set for efficacy comprised all patients who provided written informed consent and received ≥1 dose of PP3M during the treatment phase and who had at least one post-baseline efficacy assessment (modified intent-to-treat [mITT] population)

RESULTS

Patient disposition

- A total of 312 patients were screened at 57 study sites across Europe, Asia and the Middle East
- The mITT population comprised 305 patients; however, two patients withdrew at Month 3 without any post-baseline data
- The primary set for efficacy and safety analysis therefore included 303 patients
- A total of 291 patients (95.4%) completed the 12-month study

Demographics

- Baseline characteristics are presented in **Table 1**

Table 1. Baseline characteristics (modified ITT population)

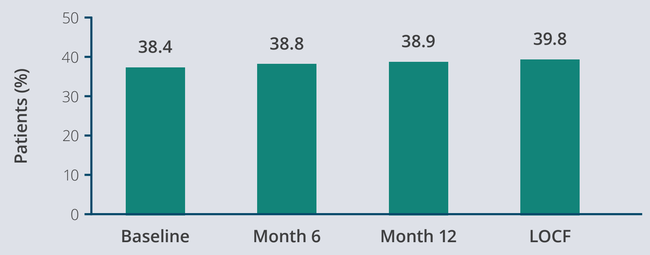
Characteristic	Total group (N=305)
Age, years	n=305
Mean (SD)	36.5 (8.0)
Median (range)	36 (20–51)
Males, n (%)	200 (65.6)
Years from schizophrenia diagnosis to study baseline	n=304
Mean (SD)	9.2 (7.3)
Median (range)	7 (0–35)
Last PP1M dose category, n (%)	n=305
50 mg	27 (8.9)
75 mg	74 (24.3)
100 mg	114 (37.4)
150 mg	90 (29.5)
Therapy prior to PP1M switch, n (%)	n=305*
Risperidone	149 (48.9)
Paliperidone	63 (20.7)
Olanzapine	24 (7.9)
Aripiprazole	9 (3.0)
Duration of previous PP1M treatment, n (%)	n=305†
4–6 months	57 (18.7)
>6 months	235 (77.0)
Patients switched from PP1M monotherapy, n (%)	253 (83.0)

**14 patients who reported to have switched from PP1M, but who withdrew early from the study, are not presented in the table. †13 patients used PP1M for at least 4 months, but the exact duration was not known. ITT: intent-to-treat; PP1M: paliperidone palmitate 1-month formulation; SD: standard deviation.*

Functional outcomes

- Functional remission was defined as achievement of PSP total score >70
  - At baseline 38.4% of patients fulfilled this criterion and this was maintained at last observation carried forward (LOCF) endpoint (39.8%) **(Figure 1)**
  - The number of patients who achieved both symptomatic (score ≤3 on PANSS items P1, P2, P3, N1, N4, N6, G5, and G9, maintained for ≥6 months[9]) and functional remission increased from Month 6 to LOCF endpoint **(Table 2)**
- Personal and social functioning (PSP total score and across all 3 domains) was maintained from baseline to endpoint **(Table 3)**

Figure 1. Achievement of functional remission



LOCF: last observation carried forward

Table 2. Achievement of symptomatic and functional remission

	Symptomatic and functional remission		
	All patients	Patients achieving SR at LOCF endpoint	Patients not achieving SR at LOCF endpoint
Baseline	-	-	-
6 months	80/297 (26.9)	74/172 (43.0)	6/125 (4.8)
12 months	89/293 (30.4)	89/172 (51.7)	0
LOCF endpoint	92/289 (31.8)	92/171 (53.8)	0

Values are n (%). LOCF: last observation carried forward; SR: symptomatic remission

Table 3. Changes in PSP score over the treatment period

	Baseline (n=294)	LOCF endpoint (n=294)	Change from baseline	95% CI of mean change from baseline
PSP total score	65.85 (14.03)	66.89 (14.28)	1.04 (11.28)	-0.3, 2.3
Social useful activities	2.62 (1.13)	2.59 (1.01)	-0.04 (0.89)	-0.1, 0.1
Personal and social relationships	2.63 (0.99)	2.59 (1.00)	-0.04 (0.85)	-0.1, 0.1
Self-care	1.79 (0.86)	1.79 (0.87)	0 (0.89)	-0.1, 0.1
Disturbing and aggressive behaviour	1.14 (0.37)	1.11 (0.40)	-0.03 (0.48)	-0.1, 0.0

Values are mean (standard deviation). CI: confidence interval; LOCF: last observation carried forward; PSP: Personal and Social Performance scale

- A good level of subjective well-being at baseline was maintained by LOCF endpoint **(Table 4)**

Table 4. Changes in SWN-S total score and subscale scores during the treatment period

	Baseline (n=297)	LOCF endpoint (n=297)	Change from baseline	95% CI of mean change from baseline
SWN-S total score	90.37 (14.23)	90.68 (15.22)	0.31 (12.51)	-1.1, 1.7
Mental functioning score	17.12 (3.67)	17.46 (3.73)	0.35 (3.50)	-0.1, 0.7
Self-control score	18.45 (3.29)	18.30 (3.36)	-0.15 (3.20)	-0.5, 0.2
Emotional regulation score	18.16 (3.56)	18.38 (3.71)	0.21 (3.37)	-0.2, 0.6
Physical functioning score	18.76 (3.67)	18.49 (3.63)	-0.27 (3.67)	-0.7, 0.1
Social integration score	17.87 (3.44)	18.05 (3.40)	0.18 (3.20)	-0.2, 0.5

This scale comprises 20 items, each scored on a 6-point Likert scale. The total score ranges from 20 (bad subjective experience) to 120 (perfect subjective experience). Values are mean (standard deviation). CI: confidence interval; LOCF: last observation carried forward; SWN-S: Subjective Wellbeing Under Neuroleptics

Patient and physician overall satisfaction with medication

- The proportion of patients satisfied (somewhat, very, extremely) with their medication showed maintenance of satisfaction at LOCF (82%) from the high baseline value (81%) **(Figure 2)**
- The proportion of physicians being overall satisfied (somewhat, very, extremely) with their patients' medication showed maintenance of overall satisfaction at LOCF (94%) from the high baseline value (96%) **(Figure 3)**

Figure 2. Patient overall satisfaction with medication at baseline and LOCF endpoint

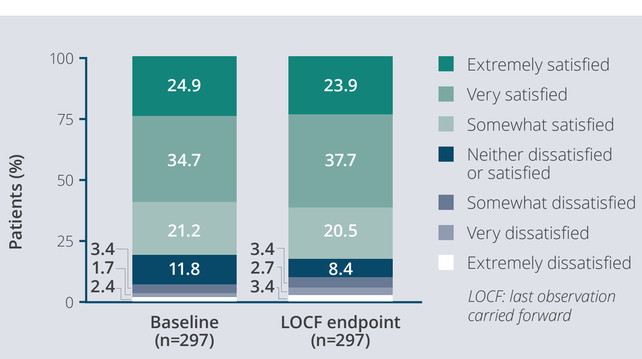
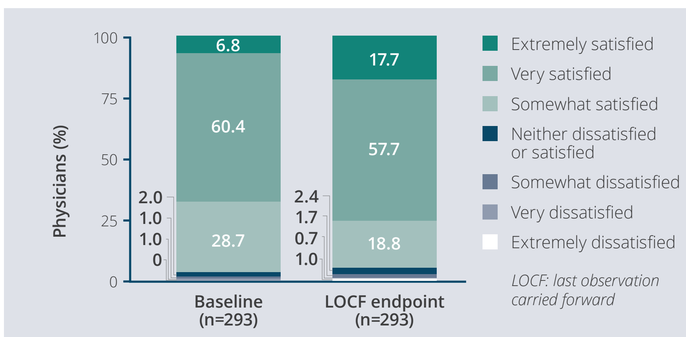


Figure 3. Physician overall satisfaction with medication at baseline and LOCF endpoint



- Mean (SD) WHODAS score decreased from 19.4 (14.7) at baseline to 16.9 (14.0) at LOCF endpoint
- Changes were observed for cognition, interacting with others, life activities and participation **(Table 5)**

Table 5. WHODAS scores at baseline and LOCF endpoint

	Baseline (n=297)	LOCF endpoint (n=297)	Change from baseline	95% CI of mean change from baseline
WHODAS total score	19.4 (14.7)	16.9 (14.0)	-2.4 (13.0)	-3.9, -0.9
Domain 1: Cognition – understanding and communicating	22.0 (18.4)	18.8 (17.1)	-3.2 (17.2)	-5.2, -1.2
Domain 2: Mobility – moving and getting around	8.8 (14.9)	8.2 (16.1)	-0.5 (14.0)	-2.2, 1.1
Domain 3: Self-care – attending to hygiene, dressing, eating and staying alone	7.2 (13.2)	5.8 (12.0)	-1.4 (13.7)	-3.0, 0.2
Domain 4: Getting along – interacting with other people	35.6 (26.7)	31.8 (24.9)	-3.9 (23.8)	-6.6, -1.1
Domain 5: Life activities – domestic responsibilities, leisure, work and school	24.3 (25.0)	20.8 (22.4)	-3.6 (24.1)	-6.3, -0.8
Domain 6: Participation – joining in community activities, participating in society	18.9 (15.3)	16.6 (15.8)	-2.3 (15.7)	-4.1, -0.5

Each of the 36 items is rated on a 5-point Likert scale where 0 = no difficulty, through to 4 = extreme difficulty/cannot perform. From the scores for all 6 domains an overall score is calculated, with higher scores indicating worse functioning (maximum score of 100). Values are mean (standard deviation). CI: confidence interval; LOCF: last observation carried forward; WHODAS: WHO Disability Assessment Schedule

- Patterns of daily activities were generally maintained from baseline to endpoint **(Table 6)**

Table 6. Quantitative assessment of daily patient activities at baseline and LOCF endpoint

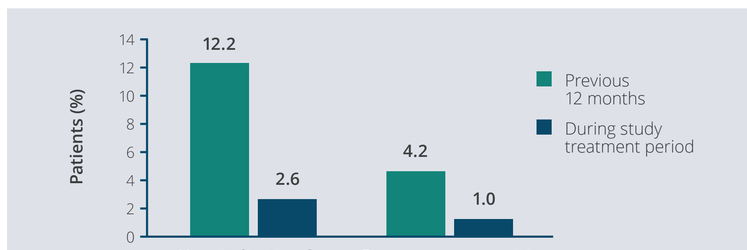
Activity category	Baseline (n=292)	LOCF endpoint (n=292)
Sleeping		
0–4 hours	2 (0.7)	8 (2.7)
4–10 hours	244 (83.6)	253 (86.6)
10 hours or more	46 (15.8)	31 (10.6)
Preparing food to eat		
0–15 minutes	137 (46.9)	119 (40.8)
15–60 minutes	133 (45.5)	155 (53.1)
60 minutes or more	22 (7.5)	18 (6.2)
Eating		
0–15 minutes	32 (11.0)	39 (13.4)
15–60 minutes	219 (75.0)	221 (75.7)
60 minutes or more	41 (14.0)	32 (11.0)
Watching TV/listening radio/internet		
0–1 hours	30 (10.3)	37 (12.7)
1–6 hours	222 (76.0)	224 (76.7)
6 hours or more	40 (13.7)	31 (10.6)
Talking on the phone/texting others		
0–15 minutes	143 (49.0)	128 (43.8)
15–60 minutes	120 (41.1)	135 (46.2)
60 minutes or more	29 (9.9)	29 (9.9)
Taking care of others		
0–1 hours	199 (68.2)	214 (73.3)
1–6 hours	86 (29.5)	71 (24.3)
6 hours or more	7 (2.4)	7 (2.4)
Working at a non-paying volunteer job		
0–1 hours	258 (88.4)	267 (91.4)
1–6 hours	27 (9.2)	23 (7.9)
6 hours or more	7 (2.4)	2 (0.7)
Exercising		
0–15 minutes	177 (60.6)	171 (58.6)
15–60 minutes	93 (31.8)	103 (35.3)
60 minutes or more	22 (7.5)	18 (6.2)
All activities with other people		
0–1 hours	107 (36.6)	111 (38.0)
1–6 hours	153 (52.4)	159 (54.5)
6 hours or more	32 (11.0)	22 (7.5)

Values are n (%). Original 7-point Likert scale responses have been aggregated into three category levels. Only those activities where there was an absolute change of ≥3% from baseline to LOCF in any category are presented.

Healthcare resource utilization

- Hospital admission and visits to the emergency department for psychiatric reasons were less frequent during the study treatment period compared with the already low incidences 12 months prior to baseline **(Figure 4)**

Figure 4. Healthcare resource utilization during the 12 months prior to study baseline and during the study treatment period



CONCLUSIONS

- Routine clinical use of PP3M in clinically stable schizophrenia patients maintained personal and social functioning scores and well-being with some incremental improvements
- The vast majority of patients and physicians were satisfied with study medication
- There was a relevant decrease in HRU over the data collection period

REFERENCES

1. Mohr P, et al. Int J Soc Psychiatry 2014;60:352–8; 2. Cichocki L, et al. Compr Psychiatry 2015;56:133–40; 3. Bellido-Zanin G, et al. Psychiatry Res 2015;230:189–93; 4. Raudino A, et al. Aust NZ J Psychiatry 2014;48:341–51; 5. Berwaerts J, et al. JAMA Psychiatry 2015;72:830–9; 6. Savitz AJ, et al. Int J Neuropsychopharmacol 2016;19:1–14; 7. Savitz AJ, et al. Int Clin Psychopharmacol 2017;32:329–36; 8. TREVICTA. Summary of Product Characteristics. June 2018; 9. Andreasen NC, et al. Am J Psychiatry 2005;162:441–9.

DISCLOSURES

This study was sponsored by Janssen. Writing and editorial assistance were provided by Michelle Preston, Cello Health MedErgy, and were funded by Janssen. P-M Llorca has received speaker and consultation fees from Janssen, EISAI, Lundbeck, Otsuka, and Bouchara-Recordatti. I Usankova, P Cherubin, and K Pungor are full-time employees of Janssen. P Bergmans is a full-time employee of Janssen and a stockholder of Johnson & Johnson. M P Garcia-Portilla has been a consultant to and/or has received honoraria/grants from Angelini, CIBERSAM, Instituto de Salud Carlos III, Janssen-Cilag, Lundbeck, Otsuka, and Pfizer. G Maina, V Bozikas, H Devrimci-Özgüven, and SW Kim have no conflicts of interest to disclose.

This poster was first presented at the 31st Congress of the European College of Neuropschopharmacology, 6-9 October 2018, Barcelona, Spain

48° Congresso Nazionale Società Italiana di Psichiatria, 13-17 Ottobre 2018, Torino, Italia