Symptomatic and Functional Remission with Paliperidone Palmitate 3-month and 6-month Formulations in Adult Patients with Schizophrenia: A 3-Year Analysis

Karen L. Johnston,[1] James Simples,[1] Ibrahim Turkoz,[2] Lisa Lim,[1*] Jose Antunes,[3] Joshua M. Hamilton,[4] Gregory Mattingly,[5] Camilo Obando[1]

[1]Janssen Scientific Affairs, LLC, Titusville, NJ, USA; [2]Janssen Research & Development, LLC, Titusville, NJ, USA; [3]Janssen-Cilag, Porto Salvo, Portugal; [4]Washington State University, College of Nursing, Department of Advanced Practice & Community-Based Care, Spokan, WA, USA; [5]St. Charles Psychiatric Associates, St. Charles, MO, USA.

Presenting author

Introduction

- Symptomatic remission is a primary treatment goal in schizophrenia; however, achieving functional remission, which reflects improved psychosocial, and vocational functioning, is critical for meaningful recovery and remains a significant challenge[1,2]
- Long-acting injectable formulations of paliperidone palmitate (PP)-1-month (PP1M) and 3-month (PP3M) have shown efficacy in maintaining low relapse rates and achieving functional remission (rates ranging from 27% to 44% based on a Personal and Social Performance [PSP] score >70)[3,4]
- With an extended dosing window of six months, the PP 6-month (PP6M) formulation has demonstrated effectiveness in preventing relapse and achieving meaningful improvements in symptomatic and functional outcomes in a 1-year double-blind (DB), noninferiority trial, with sustained benefits through a 2-year open-label extension (OLE) study[5-7]

Objectives

- To evaluate symptomatic and functional remission rates over 3-year period in patients who transitioned from PP3M to PP6M (PP3M/PP6M) or continued PP6M (PP6M/PP6M) from a 1-year noninferiority trial through a 2-year OLE study

Methods

Study Design and Patients

- This post hoc analysis utilized data from two studies: a DB, randomized, active-controlled noninferiority trial (NCT03345342)[8] and a single-arm OLE study (NCT04072575)[6]
- Patients aged 18 to 70 years with a schizophrenia diagnosis for ≥6 months and a Positive and Negative Syndrome Scale (PANSS) total score <70 were included
- The noninferiority trial involved a 28-day screening phase, open-label (OL) transition, and maintenance phases, after which, clinically stable patients on moderate/high doses of PP1M and PP3M were randomly assigned 2:1 to corresponding dorsogluteal injections of PP3M or PP6M during a 12-month DB phase (**Figure 1**)
- Eligible patients (from 6 participating countries: Argentina, Hong Kong, Italy, Poland, the Russian Federation, and Ukraine) who remained relapse-free at the end of the noninferiority trial could continue into the 2-year OLE study, receiving a total of four PP6M injections (at baseline, 6-month, 12-month, and 18-month visits)

FIGURE 1: Study design

*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. †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. ‡The OLE study was limited to 6 participating countries (Argentina, Hong Kong, Italy, Poland, the Russian Federation, and Ukraine) and enrolment was optional. 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.

Assessments

- Symptomatic remission was defined according to Andreasen's criteria[9]
  - Score ≤3 on the following 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
- Functional remission was defined as PSP score >70 at all assessment time points, with no excursion allowed
  - PSP: 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 (i.e., family, friends, partner etc.), (3) self-care such as hygiene, and (4) disturbing and aggressive behavior
  - A PSP total score between 71 and 100 indicates good functioning; a score between 31 and 70 indicates varying degrees of difficulty, and a score of ≤30 indicates poor functioning

Analysis

- 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 OLE study
- The number and percentage of patients achieving remission (symptomatic, functional, or both) at different post-baseline time points are presented by treatment group

Results

Patients

- A total of 178 patients transitioned to PP6M (PP3M/PP6M=57) or continued PP6M (PP6M/PP6M=121) from the DB phase of the noninferiority study to the OLE study

TABLE 1: Demographics and baseline characteristics (PP6M 3-year ITT)

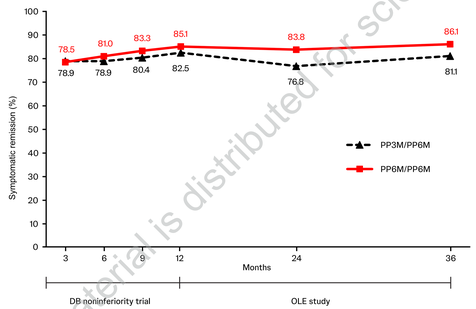
Characteristic	PP3M/PP6M (n=57)	PP6M/PP6M (n=121)
Age at NI study screening visit, years, mean (SD)	39.9 (9.69)	38.6 (11.24)
Sex, men, n (%)	43 (75.4)	83 (68.6)
Baseline BMI at NI study (OL phase), mean (SD), kg/m^2	26.9 (5.14)	27.9 (4.84)
Age at first diagnosis of schizophrenia, years, mean (SD)	29.3 (8.73)	27.5 (9.21)
PANSS score, mean (SD), DB baseline		
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)

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.

Symptomatic Remission

- At the DB endpoint (year 1), 47/57 (82.5%) PP3M/PP6M patients and 103/121 (85.1%) PP6M/PP6M patients achieved symptomatic remission
- By the OLE endpoint (year 3), 43/53 (81.1%) PP3M/PP6M patients and 87/101 (86.1%) PP6M/PP6M patients maintained symptomatic remission

FIGURE 2: Proportion of patients achieving symptomatic remission through the 3-year study period (ITT population)

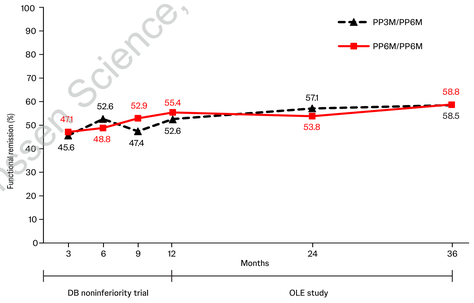


DB, double-blind; ITT, intent-to-treat; OLE, open-label extension; PP3M, paliperidone palmitate 3-month formulation; PP6M, paliperidone palmitate 6-month formulation.

Functional Remission

- At the DB endpoint (year 1), 30/57 (52.6%) PP3M patients and 67/121 (55.4%) PP6M patients achieved functional remission
- By the OLE endpoint (year 3), 31/53 (58.5%) PP3M/PP6M patients and 60/102 (58.8%) PP6M/PP6M patients maintained functional remission

FIGURE 3: Proportion of patients achieving functional remission through the 3-year study period (ITT population)

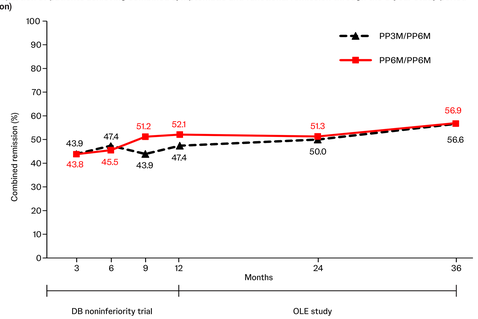


DB, double-blind; ITT, intent-to-treat; OLE, open-label extension; PP3M, paliperidone palmitate 3-month formulation; PP6M, paliperidone palmitate 6-month formulation.

Combined Remission

- At the DB endpoint (year 1), 27/57 (47.4%) PP3M/PP6M patients and 63/121 (52.1%) PP6M/PP6M patients met the criteria for both symptomatic and functional remission
- By the OLE endpoint (year 3), 30/53 (56.6%) PP3M/PP6M patients and 58/102 (56.9%) PP6M/PP6M patients met the criteria for both symptomatic and functional remission

FIGURE 4: Proportion of patients achieving combined symptomatic and functional remission through the 3-year study period (ITT population)



DB, double-blind; ITT, intent-to-treat; OLE, open-label extension; PP3M, paliperidone palmitate 3-month formulation; PP6M, paliperidone palmitate 6-month formulation.

Conclusions

- 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 long-term efficacy of these treatments
- A high proportion (>56%) of patients who transitioned from PP3M to PP6M or continued PP6M treatment had sustained symptomatic and functional remission
- These findings support the long-term efficacy of PP3M and PP6M, highlighting the benefits of transitioning to longer acting antipsychotic formulations in achieving and sustaining both symptomatic stability and functional improvement in adult patients with schizophrenia
- 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

Acknowledgements

The authors thank the study patients and investigators for their participation. Priya Ganpathy, MPH CMPP (SIRO Clinpharm UK Limited) provided medical writing assistance and Ellen Baum, PhD (Janssen Global Services, LLC) provided additional editorial support. Sandeep Chavan (SIRO Medical Writing Pvt. Ltd.) provided graphic designing support.

Disclosures

KLJ, JS, IT, LL and CO are employees of Janssen Scientific Affairs, LLC and stockholders of Johnson & Johnson. JA is an employee of Janssen-Cilag, Portugal (a Johnson & Johnson company) 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, and Teva. JH is a psychiatric nurse practitioner and is a consulting speaker for Tempus AI, Inc. and a consultant for the Point of Care Network.

Neuropsychiatry

Please scan the QR code

The QR code is intended to provide scientific information for individual reference, and the information should not be altered or reproduced in any way.

https://www.congresshub.com/Neuroscience/PsychCongress2024/PaliperidonePalmitate/Johnston

Poster presented at the Psych Congress, 2024, October 29 to November 02 | Boston, MA USA

REFERENCES:

1. Correll CU, et al. Schizophrenia (Heidelb). 2023;9:80; **2.** Valencia M, et a. Neuropsychiatr Dis Treat. 2015;11:2339–2348; **3.** Savitz AJ, et al. Int Clin Psychopharmacol. 2017;32:329-336; **4.** Mathews M, et al. Neuropsychiatr Dis Treat. 2019;15:1365–1379; **5.** Najarian D, et al. Int J Neuropsychopharmacol. 2022;25:238-251; **6.** Najarian D, et al. Int J Neuropsychopharmacol. 2023; pyad028; **7.** Correll CU, et al. JAMA Netw Open. 2024;7:e2421495; **8.** Andreasen NC, et al. Am J Psychiatry. 2005;162:441–449.