Symptomatic Remission with Paliperidone Palmitate 3-Monthly Formulation in Schizophrenia Patients in Clinical Practice Setting: REMISSIO

Maria Paz Garcia-Portilla1, Pierre-Michel Llorca2, Giuseppe Maina3, Vasili P Bozikas4, Halise Devrimci-Ozguven5, Kim Sung Wan6, Paul Bergmans7, Irina Usanokva7, Pierre Cherubin8, Katalin Pungr8

1SCDU Psichiatria, AOU San Luigi Gonzaga, Università degli Studi di Torino, Italy; 2Department of Psychiatry, School of Medicine, Ankara University, Turkey; 3Department of Psychiatry, School of Medicine, Ankara University, Ankara, Turkey; 4Psychiatry Department, University of Athens, Athens, Greece; 5Psychiatric Clinic, University of Pisa, Pisa, Italy; 6Department of Psychiatry, Seoul National University College of Medicine, Seoul National University Hospital, Seoul, South Korea; 7Department of Psychopharmacology, University of Antwerp, Antwerp, Belgium; 8University of Geneva, Geneva, Switzerland

INTRODUCTION

In patients with schizophrenia, achievement of symptomatic remission (G2S; defined as low levels of selected symptoms maintained for ≥6 months) predicts improvement in psychosocial functioning and quality of life.1,2 Long-acting injectable paliperidone palmitate 3-month formulation (PP3M) administered four times a year, is approved for use in the USA, Canada, the EU, and Japan.3,4 In Asian countries as maintenance treatment for patients with schizophrenia whose symptoms have been stabilized with paliperidone palmitate 1-month formulation (PP1M)5

In two pivotal randomized clinical trials, PP3M demonstrated favorable efficacy and tolerability in schizophrenia6,7 in the non-inferiority trial comparing PP3M and PP1M, 50% of patients achieved SR in the final 6 months of the double-blind treatment phase.8 However, due to the selective nature of randomized clinical trials, results from these trials may not be entirely representative of the diverse population of schizophrenia patients in real life.

OBJECTIVE

To assess the impact of the transition from PP1M to PP3M in patients with clinically stable schizophrenia in a real-world setting, with a primary objective of assessing the percentage of patients achieving SR at study endpoint.

METHODS

Study design

An international prospective Phase III, single-arm, non-randomized, open-label, 52-week study conducted in a diverse population of patients with schizophrenia seen in clinical practice (REMISSIO study, ClinicalTrials.gov identifier NCT02713282) in patients previously stabilized on PP1M treatment. 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 clinician’s discretion) were made according to the product label.

Patients

Patients aged 18–50 years with a confirmed diagnosis of schizophrenia (Diagnostic and Statistical Manual of Mental Disorders, 5th Edition) were included.

Patients who previously switched from PP1M to PP3M were allowed to participate in the study.

A baseline Positive and Negative Syndrome Scale (PANSS) total score ≥70 was required.

Assessments

Assessments were made at 3-monthly intervals during the treatment period.

A follow-up call for safety assessments was made 3 months after Month 12 or 3 months after early study discontinuation.

Outcomes

The primary outcome was the number of patients who achieved SR (defined as low levels of selected symptoms maintained for ≥6 months) at the last observation carried forward (LOCF) endpoint (Month 12 or early discontinuation).

Main secondary outcomes included changes in PANSS total and subscores, PANSS Marder factors, Clinical Global Impression of Severity (CGI-S), Clinical Global Impression of Change (CGI-C) and adverse events (AEs).

The primary analysis set for efficacy and safety comprised all patients who provided written informed consent and received at least one dose of PP3M during the treatment phase and who had at least one 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 who were randomly assigned were not enrolled and therefore were not included in the safety analyses.

A total of 291 (95.4%) patients completed the 12-month study.

Demographics

Baseline characteristics are presented in Table 1.

Table 1. Baseline characteristics modified (ITT population)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total group (% N=312)</th>
<th>mITT population (% N=305)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>35 (3–50)</td>
<td>35 (3–50)</td>
</tr>
<tr>
<td>Male (%)</td>
<td>55.3</td>
<td>55.4</td>
</tr>
<tr>
<td>Race (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Other</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>25.8 (5.3)</td>
<td>25.6 (5.3)</td>
</tr>
<tr>
<td>PANSS (score)</td>
<td>73.9 (16.9)</td>
<td>73.7 (16.8)</td>
</tr>
<tr>
<td>Baseline SR (%)</td>
<td>22.8</td>
<td>22.7</td>
</tr>
</tbody>
</table>

DISCUSSION

Efficacy outcomes

At LOCF endpoint, 67.8% of patients were considered to have improved, according to the CGI-C (Figure 4).

Safety

A total of 161 patients in the mITT (G2S) population reported at least one treatment-emergent adverse event (TEAE).

Table 3. Treatment-emergent adverse events experienced by ≥2% of patients

Table 2. PANSS scores at baseline and LOCF endpoint

CONCLUSIONS

For the majority of clinically stable patients with schizophrenia, converting from PP1M in a naturalistic setting, PP3M achieved SR and maintained symptom stability.

In this patient population of mild/moderate symptomatology, around 68% of the participants showed improvement according to the CGI-C.

The completion rate of 95.4% is one of the highest ever observed for a 1-year study in schizophrenia, with a low number of discontinuations due to AEs in both groups.1,9

PP3M was generally well tolerated.

Results from this naturalistic study were similar to those observed in randomized clinical trials for PP3M, and underline the importance of continuous treatment in patients with schizophrenia.

REFERENCES


DISCLOSURES

This study was sponsored by Janssen. Writing and editorial assistance were provided by Michelle Peterson, Celso N. Medeiros Maldague, and were funded by Janssen-P Michel Lorca received speaker and consultation fees from Janssen, EISAI, Lundbeck, and Neuralex. J P Bergmans is a full-time employee of Janssen and a stockholder of Janssen & Janssen. V P Bozikas is a consultant and/or has received honoraria/agents from angles, CERESAM, Instituto de Salud Carlos III, Janssen-Glax, Lundbeck, Otsuka, and Pfizer. G Maina, V Buglass, H Devrimci, Ozguven, and O M Kim have no conflicts of interest to disclose.

Figure 3. Clinical Global Impression of Severity at baseline and LOCF endpoint

Figure 4. Clinical Global Impression of Change at LOCF endpoint

PANO: Positive and negative symptomatology