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

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**INTRODUCTION**

- In patients with schizophrenia, achievement of symptomatic remission (OR) defined as low levels of selected symptoms measured for at least 6 months predicts improvement in psychosocial functioning and quality of life.
- Long-acting injectable paliperidone palmitate 3-month formulation (PP3M), administered every four months, is approved for use in the USA, Canada, the EU and several Asian countries as maintenance treatment for patients with schizophrenia whose symptoms have been stabilized with paliperidone palmitate 1-month formulation (PP1M).
- In two pooled randomized controlled trials, PP3M demonstrated favorable efficacy and tolerability in schizophrenia
- 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.
- However, due to the selective nature of randomized clinical trials, results from the 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 IIIb, single-arm, non-randomized, open-label, pragmatic, real-world study
- The primary endpoint was achievement of SR defined as ≤3 on PANSS it or at 3 months after early study discontinuation
- Patients
  - Patients aged 18–50 years with a confirmed diagnosis of schizophrenia (Diagnostic and Statistical Manual of Mental Disorders, 5th Edition)
  - Adequate treatment with PP1M for ≥4 months (the last two doses of PP1M being separated by >5 weeks)
  - A baseline Positive and Negative Syndrome Scale (PANSS) total score ≥70

**Assessments**

- Assessments were made at 3-month 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 (score ≤3) on PANSS items P1, P2, P3, N1, N4, N6, and G6, maintained for ≥6 months in 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 Change (CGI-C), Clinical Global Impression of Change (CGI-I) and adverse events (AEs)
- The primary analysis set for efficacy and safety comprised all patients who provided written informed consent and reached at least one 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 13 without any post-baseline data.
- The primary set for efficacy and safety analysis therefore included 303 patients.
- A total of 291 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=303)</th>
<th>Baseline completers (n=291)</th>
<th>LOCF endpoint (n=303)</th>
<th>Mean change (±SEM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>39.5 (7.9)</td>
<td>41.4 (7.7)</td>
<td>40.1 (7.8)</td>
<td>-1.2 (0.1)</td>
</tr>
<tr>
<td>Median weight</td>
<td>86 (0.0–137)</td>
<td>84 (0.0–137)</td>
<td>86 (0.0–137)</td>
<td>-1.1 (0.0)</td>
</tr>
<tr>
<td>Years from schizophrenia diagnosis to baseline</td>
<td>6.9 (4.7)</td>
<td>6.9 (4.7)</td>
<td>6.9 (4.7)</td>
<td>0.2 (0.1)</td>
</tr>
<tr>
<td>Median change</td>
<td>1.0 (0.0–8.0)</td>
<td>1.0 (0.0–8.0)</td>
<td>1.0 (0.0–8.0)</td>
<td>0.0 (0.0)</td>
</tr>
<tr>
<td>Last PP1M dose category, n (%)</td>
<td>55.4</td>
<td>55.7</td>
<td>55.4</td>
<td>0.1</td>
</tr>
<tr>
<td>Total treatment period (n, %)</td>
<td>252 (83.2)</td>
<td>245 (84.0)</td>
<td>252 (83.2)</td>
<td>0.2</td>
</tr>
<tr>
<td>Last PP1M dose category (n)</td>
<td>105 (34.7)</td>
<td>106 (37.4)</td>
<td>105 (34.7)</td>
<td>0.7</td>
</tr>
<tr>
<td>Total treatment period (n, %)</td>
<td>252 (83.2)</td>
<td>245 (84.0)</td>
<td>252 (83.2)</td>
<td>0.2</td>
</tr>
<tr>
<td>Baseline weight, n (%)</td>
<td>86.0 (137.7)</td>
<td>84.0 (137.7)</td>
<td>86.0 (137.7)</td>
<td>0.0 (0.0)</td>
</tr>
<tr>
<td>Endpoints of previous PP1M treatment, n (%)</td>
<td>4 (1.3)</td>
<td>4 (1.3)</td>
<td>4 (1.3)</td>
<td>0.0</td>
</tr>
<tr>
<td>Duration of previous PP1M treatment, n (%)</td>
<td>6–12 months</td>
<td>6–12 months</td>
<td>6–12 months</td>
<td>0.0</td>
</tr>
<tr>
<td>Weight decreased, n (%)</td>
<td>10 (3.3)</td>
<td>10 (3.3)</td>
<td>10 (3.3)</td>
<td>0.4</td>
</tr>
<tr>
<td>Weight increased, n (%)</td>
<td>11 (3.6)</td>
<td>11 (3.6)</td>
<td>11 (3.6)</td>
<td>0.5</td>
</tr>
<tr>
<td>Adverse event, n (%)</td>
<td>150 (49.4)</td>
<td>149 (48.9)</td>
<td>150 (49.4)</td>
<td>0.1</td>
</tr>
<tr>
<td>Total upper respiratory tract infection</td>
<td>11 (3.6)</td>
<td>11 (3.6)</td>
<td>11 (3.6)</td>
<td>0.0</td>
</tr>
<tr>
<td>Infections</td>
<td>50 (16.5)</td>
<td>50 (16.5)</td>
<td>50 (16.5)</td>
<td>0.0</td>
</tr>
<tr>
<td>Schizophrenia</td>
<td>10 (3.3)</td>
<td>10 (3.3)</td>
<td>10 (3.3)</td>
<td>0.0</td>
</tr>
<tr>
<td>Weight decreased</td>
<td>10 (3.3)</td>
<td>10 (3.3)</td>
<td>10 (3.3)</td>
<td>0.0</td>
</tr>
</tbody>
</table>

**Treatment exposure**

- Mean (SD) follow-up was 53.7 (SD: 32.3) days and duration of exposure was 25.1 (42.4) days
- Doses of PP3M received remained stable during the treatment period
- The 12-month study period included 184 patients achieved SR
- Five patients had met the SR at Month 9 (loss at Month 9) and 7 who achieved SR at Month 9 (lost at Month 12)
- The Kaplan–Meier estimate of median time to achievement of SR was 247 days (95% CI 189–275)
- At baseline, 156 patients (51%) met the PANSS severity criterion for remission at baseline and the Kaplan–Meier estimate of median time to achievement of SR was 247 days (95% CI 189–275)
- Five patients who met the SR at Month 6 lost SR at Month 9

**Efficacy outcomes**

- At LOCF endpoint, 73.0% of patients (65.4%; 95% confidence interval [CI] 51.0–62.4%) had achieved SR
- During the 12-month study period, 73.0% of patients achieved SR
- Five patients had met the SR at Month 9 (loss at Month 9) and 7 who achieved SR at Month 9 (lost at Month 12)
- The Kaplan–Meier estimate of median time to achievement of SR was 247 days (95% CI 189–275)

**Safety**

- A total of 160 patients in the MITT (31%) reported at least one treatment-emergent adverse event (TEAE)
- 81 (16.5%) patients reported a TEAE that was at least possibly related to study medication
- 14 patients (4.9%) experienced at least one possibly related TEAE that with the product label

**DISCUSSIONS**

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**REFERENCES**


**CONCLUSIONS**

- For the majority of clinically stable patients with schizophrenia, converting from PP1M to 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 99.4% is one of the highest ever observed for a 1-year study in schizophrenia, with a low number of discontinuations due to AEs or patient withdrawals
- 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.

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