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Stable Schizophrenia Patients Switched to Paliperidone Palmitate 3-Monthly Formulation in Real Life: Impact of Patient Age on Outcomes

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INTRODUCTION

- Schizophrenia is a complex and heterogeneous mental disorder[1]. Continuous maintenance treatment with antipsychotics is essential for effective symptom control, relapse prevention and good functioning[2,3]
- Paliperidone palmitate 3-monthly formulation (PP3M) is a long-acting, injectable antipsychotic treatment approved in many countries worldwide for the maintenance treatment of adult patients with schizophrenia stabilized on paliperidone palmitate 1-monthly formulation (PP1M)[4]
- The REMISSIO phase 3b study evaluated the efficacy and safety of converting patients with schizophrenia stabilized with PP1M to PP3M in a naturalistic clinical setting[5]

OBJECTIVE

- This *post hoc* subgroup analysis of the REMISSIO dataset assessed differences in outcomes between younger (aged <35 years) and older (aged ≥35 years) patients with schizophrenia treated with PP3M

METHODS

Study design

- An international, prospective, Phase 3b, single-arm, open-label, 52-week study conducted in a diverse population of patients with schizophrenia seen in clinical practice (ClinicalTrials.gov: 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 (at clinicians' discretion) were made in line with the product label[4]

Participants

- Patients aged 18–50 years with a diagnosis of schizophrenia, adequately treated with PP1M for at least 4 months (with two identical doses before switching) with a baseline Positive and Negative Syndrome Scale (PANSS) total score of <70

Assessments

- The primary study outcome was the proportion of patients who achieved symptomatic remission (SR) following 52 weeks of treatment[5], as defined by the Andreasen criteria: score of ≤3 for 8 key PANSS items (P1, P2, P3, N1, N4, N6, G5, G9) maintained for a minimum of 6 months[6]
- Secondary outcomes included changes in PANSS Total, Subscale and Marder factor scores, Clinical Global Impression – Severity (CGI-S) and Change (CGI-C), Personal and Social Performance (PSP), functional remission (PSP total score >70) (efficacy populations) and hospitalizations for psychiatric reasons (modified intent-to-treat population)
- Safety evaluations included assessment of treatment-emergent adverse events (TEAEs), extrapyramidal symptoms, weight and body mass index (BMI) change and vital signs

RESULTS

Patient demographics/disease characteristics at baseline

- Patients aged <35 years and ≥35 years (n=123, mean age: 28.5 years, and n=182, mean age: 41.9 years, respectively; modified intent-to-treat population) were included in this subgroup analysis (**Table 1**)
- Patient demographics were broadly similar; however, there was a higher proportion of males in the younger group (75.6% vs 58.8%)
- Patient disease characteristics, including psychiatric history, were more severe in the older group

Table 1. Baseline demographics and disease characteristics

Patient demographics/disease characteristics	Patient age	
	<35 years (n=123)	≥35 years (n=182)
Age (years)	28.5 (3.8)	41.9 (4.9)
Sex, male (%)	75.6	58.8
BMI (kg/m^2)	26.7 (5.5)	27.9 (4.9)
Therapy prior to PP1M switch, n (%):		
Risperidone	55 (45.8)	94 (55)
Paliperidone	27 (22.5)	36 (21.1)
Psychiatric history obtained, n (%)	123 (100.0)	181 (99.5)
Years since schizophrenia diagnosis*	5.4 (4.2)	11.9 (7.8)
Years since first antipsychotic use*	6.1 (4.4)	13.1 (7.3)
Patient has been previously hospitalized for psychiatric reasons, n (%)	103 (83.7)	152 (84.0)
Total number of psychiatric hospitalizations*	2.5 (2.4)	3.8 (4.5)
Years since first hospitalization*	5.3 (4.2)	11.4 (7.9)
Suicide attempts since diagnosis*, n (%)	9.0 (7.3)	14 (7.7)

Modified intent-to-treat population
Values are mean (standard deviation) unless otherwise stated
*To baseline visit

Study completion, PP3M exposure and dosing (modified intent-to-treat population)

- Study completion rates were above 95% for both groups
- PP3M exposure and dosing was similar in both age groups (**Table 2**)

Table 2. Study completion rate, PP3M exposure and dosing

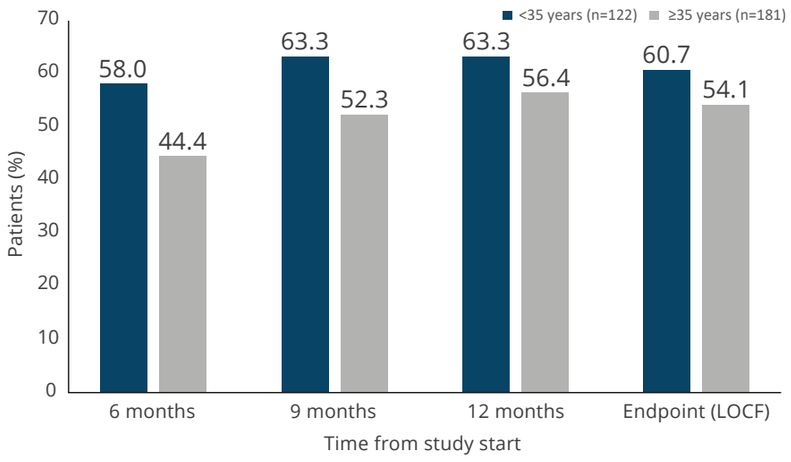
Parameter	Patient age	
	<35 years (n=123)	≥35 years (n=182)
Completed follow-up, n (%)	118 (95.9)	173 (95.1)
Exposure duration, days, mean (SD)	262.8 (42.2)	263.1 (42.8)
Follow-up time duration, days, mean (SD)	352.4 (56.9)	352.8 (49.1)
Average dose during follow-up, mg, mean (SD)	364.6 (111.6)	363.2 (119.2)

Modified intent-to-treat population. SD, standard deviation

Symptomatic remission

- A higher proportion of younger versus older patients reached SR (95% confidence interval [CI]) at the last observation carried forward (LOCF) endpoint: 60.7 (51.4, 69.4)% vs 54.1 (46.6, 61.6)% (**Figure 1**)
- Median (95% CI) time to SR was shorter for younger versus older patients at the LOCF endpoint 189 (184, 262) days vs 273 (191, 364) days. However, the difference between the two groups was not statistically significant

Figure 1. Symptomatic remission during follow-up and at LOCF endpoint



PANSS: Total and Subscale scores

- PANSS Total (**Figure 2**) and Subscale (**Table 3**) scores indicated a significant reduction in disease severity from baseline to LOCF endpoint during the follow-up period in both age groups
- The greatest improvements from baseline to LOCF endpoint for PANSS Subscale scores in both groups were in the Negative and General Subscales (**Table 3**)

Figure 2. PANSS Total score: baseline to LOCF endpoint

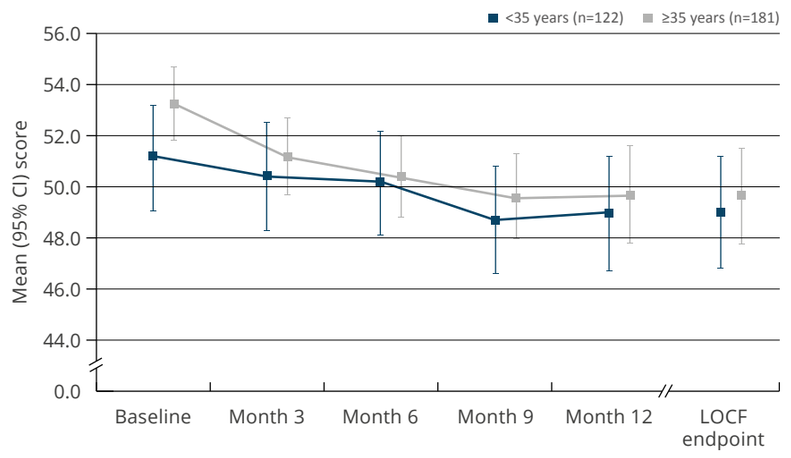


Table 3. PANSS Subscale scores: change from baseline to LOCF endpoint

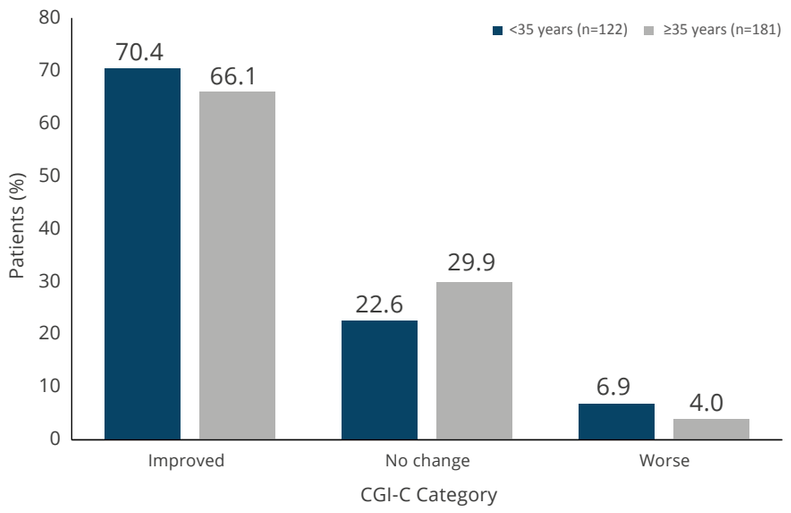
Parameter	Patient age	
	<35 years (n=122)	≥35 years (n=181)
PANSS Positive Subscale	-0.5 (-1.1, 0.1)	-0.9 (-1.3, -0.6)
PANSS Negative Subscale	-0.9 (-1.5, -0.3)	-1.3 (-1.8, -0.7)
PANSS General Subscale	-0.9 (-1.7, -0.1)	-1.4 (-2.3, -0.6)

Efficacy population; values are mean (95% CI) change from baseline
Only subjects with both baseline and ≥1 post-baseline assessments included in analysis

Clinical Global Impression

- Mean (95% CI) changes in CGI-S from baseline to LOCF endpoint for younger and older patients were -0.1 (-0.3, 0.1) and -0.2 (-0.3, -0.1), respectively, indicating a reduction in disease severity
- A slightly higher proportion of younger (70.4%) versus older patients (66.1%) had improved CGI-C scores at LOCF endpoint (**Figure 3**)

Figure 3. CGI-C: frequency distribution score categories at LOCF endpoint

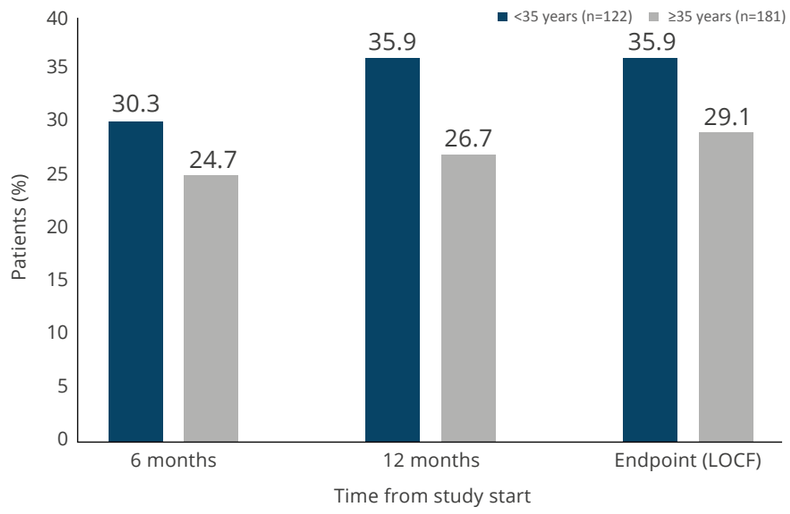


'Improved' is a composite of the categories 'very much improved', 'much improved' and 'minimally improved'; 'Worse' is a composite of the categories 'minimally worse' and 'much worse'

Personal and Social Performance Scale

- A higher proportion of younger patients achieved functional remission (PSP score 71–100) compared with older patients, both at baseline (43.7% vs 34.9%) and LOCF endpoint (45.4% vs 36.0%)
- The proportion of patients with moderate functioning (PSP score 31–70) was lower in the younger vs older patient groups: 54.6% vs 64.0% at baseline and 52.1% vs 61.1% at LOCF endpoint
- The proportion of patients with poor functioning (PSP score ≤30) was low in both the younger and older patient groups: 1.7% vs 1.1% at baseline and 2.5% vs 2.9% at LOCF endpoint
- A substantial proportion of patients achieved SR as well as functional remission at LOCF endpoint in both age groups (35.9% and 29.1% for patients <35 years and ≥35 years, respectively) (**Figure 4**)

Figure 4. Symptomatic and functional remission during follow-up and at LOCF endpoint*

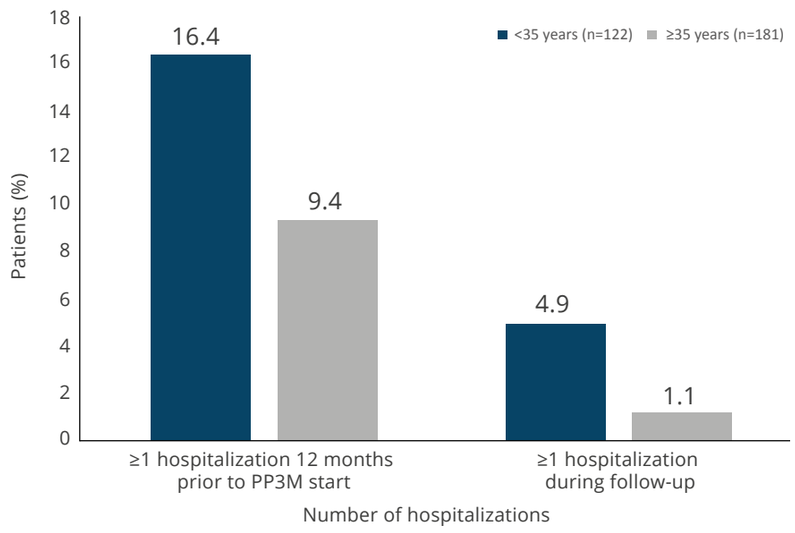


*Month 9 data are not available as PSP assessments were performed at Months 6 and 12

Hospitalization due to psychiatric reasons

- Hospitalizations for psychiatric reasons 12 months before initiation of PP3M were higher for younger compared with older patients (16.4% vs 9.4%); hospitalizations fell sharply during the year after PP3M initiation in both groups (4.9% vs 1.1%) (**Figure 5**)

Figure 5. Hospitalizations for psychiatric reasons: prior to PP3M initiation and during follow-up



Safety

- TEAE profiles were similar in the two age groups with low numbers (2 cases in both groups: 1.6% vs 1.1%) leading to study discontinuation (**Table 4**)
- The most common drug-related TEAEs were the same in both age groups (<35 vs ≥35 years): psychiatric disorders (9.0% vs 5.5%), general disorders/administration site conditions (9.0% vs 7.2%), weight change (9.0% vs 9.4%) and nervous system disorders (8.2% vs 9.9%)
- Rates of TEAEs of interest, including potentially prolactin-related TEAEs, were similar between the two age groups
- Mean (standard deviation) change from baseline to LOCF endpoint in the Extrapyramidal Symptoms Rating Scale total score was −0.80 (2.38) and −0.62 (2.14) in the <35 years and ≥35 years groups, respectively

Table 4. Summary of treatment-emergent adverse events

Number of patients, n (%), with at least one:	Patient age	
	<35 years (n=122)	≥35 years (n=181)
TEAE leading to treatment/study discontinuation	2 (1.6)	2 (1.1)
Serious TEAE	8 (6.6)	10 (5.5)
Probable/very likely drug-related TEAE	40 (32.8)	51 (28.2)

Safety population

CONCLUSIONS

- The results from this exploratory *post hoc* analysis suggest that while improvements in disease severity and symptom control were noted in both age groups, switching from PP1M to PP3M treatment may more positively impact younger patients with schizophrenia compared with older patients
- Study completion rates were above 95% for both groups
- Safety profiles after 52 weeks of PP3M treatment were comparable in the two age groups
- These data support early switching to PP3M treatment in real-world clinical practice[5,7-9]
- Further long-term studies examining the efficacy and safety of PP3M in younger versus older adult patients with schizophrenia are warranted

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DISCLOSURES

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